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(54) Title: 1 - (HETEROARYL-PHENYL) - CONDENSED PYRAZOL DERIVATIVES AS FACTOR XA INHIBITORS

(57) Abstract: The present application describes heteroaryl-phenyl heterobicycles and derivatives thereof, or pharmaceutically acceptable salt forms thereof, which are useful as inhibitors of factor Xa.

TITLE

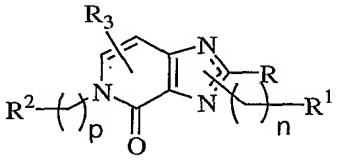
1-(HETEROARYL-PHENYL)-CONDENSED PYRAZOL DERIVATIVES AS FACTOR XA INHIBITORS

FIELD OF THE INVENTION

This invention relates generally to heteroaryl-phenyl heterobicyclic compounds, which are inhibitors of trypsin-like serine protease enzymes, especially factor Xa, pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

BACKGROUND OF THE INVENTION

WO00/20416 and WO00/40583 describe imidazole[4,3-c]-pyridin-4-one compounds of the following formula.



These compounds are stated to be factor Xa inhibitors. Compounds of this type, however, are not considered to be part of the presently claimed invention.

Activated factor Xa, whose major practical role is the generation of thrombin by the limited proteolysis of prothrombin, holds a central position that links the intrinsic and extrinsic activation mechanisms in the final common pathway of blood coagulation. The generation of thrombin, the final serine protease in the pathway to generate a fibrin clot, from its precursor is amplified by formation of prothrombinase complex (factor Xa, factor V, Ca^{2+} and phospholipid). Since it is calculated that one molecule of factor Xa can generate 138 molecules of thrombin (Elodi, S., Varadi, K.: Optimization of conditions for the catalytic effect of the factor IXa-factor VIII Complex: Probable role of the complex in the amplification of blood

coagulation. *Thromb. Res.* **1979**, *15*, 617-629), inhibition of factor Xa may be more efficient than inactivation of thrombin in interrupting the blood coagulation system.

Therefore, efficacious and specific inhibitors of factor Xa are needed as potentially valuable therapeutic agents for the treatment of thromboembolic disorders. It is thus desirable to discover new factor Xa inhibitors.

SUMMARY OF THE INVENTION

Accordingly, one object of the present invention is to provide novel heteroaryl-phenyl heterobicyclic compounds that are useful as factor Xa inhibitors or pharmaceutically acceptable salts or prodrugs thereof.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide a method for treating thromboembolic disorders comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide novel heteroaryl-phenyl heterobicyclic compounds for use in therapy.

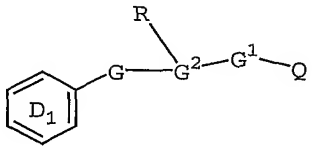
It is another object of the present invention to provide the use of novel heteroaryl-phenyl heterobicyclic compounds for the manufacture of a medicament for the treatment of a thromboembolic disorder.

These and other objects, which will become apparent during the following detailed description, have been achieved by the inventors' discovery that the presently

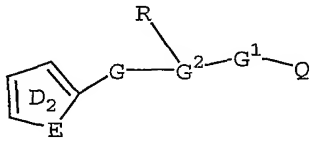
claimed heteroaryl-phenyl heterobicyclic compounds, or pharmaceutically acceptable salt or prodrug forms thereof, are effective factor Xa inhibitors.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

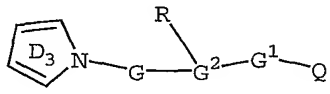
[1] Thus, in a first embodiment, the present invention provides a novel compound of formula Ia, Ib, or Ic:



Ia



Ib



Ic

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

ring D_1 is selected from pyridine, pyrazine, pyridazine, and pyrimidine and is substituted with 1 R^a and 0-1 R^b;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-3 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^a is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^b is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^c is selected from H, C_{1-4} alkyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

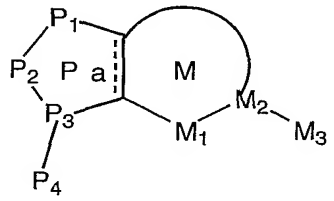
G is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$;

G_1 is absent or is selected from $(CR^3R^{3a})_{1-5}$, $(CR^3R^{3a})_{0-2}CR^3=CR^3(CR^3R^{3a})_{0-2}$, $(CR^3R^{3a})_{0-2}C\equiv C(CR^3R^{3a})_{0-2}$, $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)O(CR^3R^{3a})_w$, $(CR^3R^{3a})_uOC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uO(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uOC(O)NR^3(CR^3R^{3a})_w$,

$(CR^3R^{3a})_uNR^3C(O)O(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(S)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3S(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2NR^3(CR^3R^{3a})_w$, and $(CR^3R^{3a})_uNR^3S(O)_2NR^3(CR^3R^{3a})_w$, wherein u + w total 0, 1, 2, 3, or 4, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

G^2 is phenyl, naphthyl, or a 5-10 membered heteroaryl consisting of carbon atoms and from 1-3 heteroatoms selected from N, O, and S;

Q is a group of formula II:



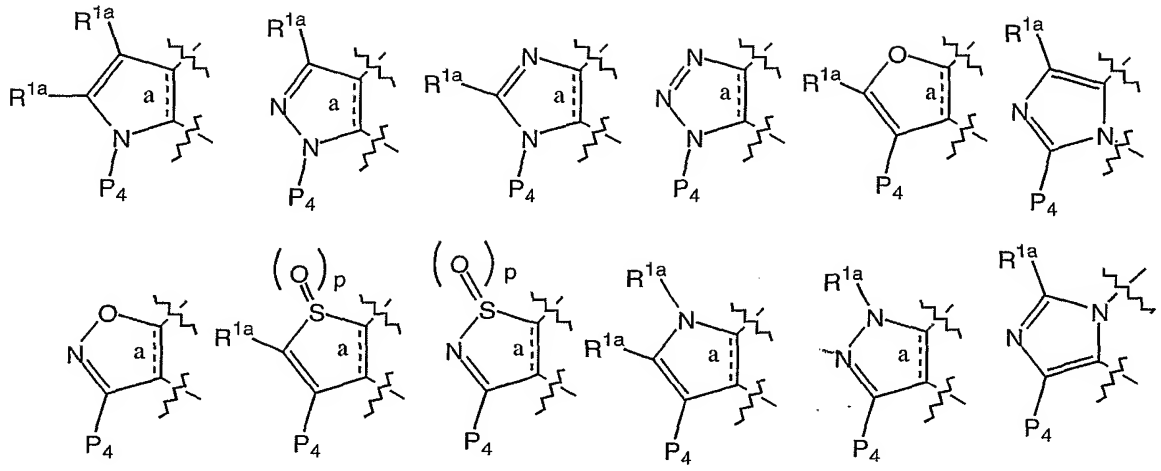
II

one of P_4 and M_3 is -Z-A-B and the other is attached to G_1;

ring M, including M_1 and M_2, is a 6 or 7 membered carbocycle or 6 or 7 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, $S(O)_p$, N, and NZ^2;

ring M is substituted with 0-2 R^{1a} and 0-2 carbonyl groups, and, comprises: 0-2 additional double bonds;

ring P, including P_1, P_2, P_3, and P_4 is selected from group:



"a" is absent or is a bond

provided that when Q is a dihydroimidazolo[4,5-c]-pyridin-4-one then:

(i) G_1 is present and is other than alkylene;

(ii) Z is present and is other than alkylene;

(iii) Ring D_1-G is present, D_1-G is other than benzyloxy;

(iv) Ring D_3 is present; or

(v) Ring D_2 is present and is other than 5-methyl-1,2,4-oxadiazole or 5-oxo-1,2,4-oxadiazole;

Z is selected from a bond, $-(CR^2R^{2a})_{1-4}-$, $(CR^2R^{2a})_qO(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)_2(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qSO_2NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3SO_2(CR^2R^{2a})_{q^1}$, and $(CR^2R^{2a})_qNR^3SO_2NR^3(CR^2R^{2a})_{q^1}$, wherein $q + q^1$ total 0, 1, or 2, provided that Z does

not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

Z^2 is selected from H, C_{1-4} alkyl, phenyl, benzyl, $C(O)R^3$, and $S(O)_pR^{3c}$;

R^{1a} is selected from H, $-(CH_2)_r-R^{1b}$, $-CH=CH-R^{1b}$, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $NH(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, $S(O)_p(CH_2)_rR^{1d}$, $O(CH_2)_rR^{1d}$, $NR^3(CH_2)_rR^{1d}$, $OC(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)O(CH_2)_rR^{1d}$, and $NR^3C(O)(CH_2)_rR^{1d}$, provided that R^{1a} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

alternatively, when two R^{1a}'s are attached to adjacent atoms, together with the atoms to which they are attached they form a 5-7 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$, this ring being substituted with 0-2 R^{4b} and comprising: 0-3 double bonds;

R^{1b} is selected from H, C_{1-3} alkyl, F, Cl, Br, I, -CN, -CHO, $(CF_2)_rCF_3$, $(CH_2)_rOR^2$, NR^2R^{2a}, $C(O)R^{2c}$, $OC(O)R^2$, $(CF_2)_rCO_2R^{2a}$, $S(O)_pR^{2b}$, $NR^2(CH_2)_rOR^2$, $C(=NR^{2c})NR^2R^{2a}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NHR^{2b}$, $NR^2C(O)_2R^{2a}$, $OC(O)NR^{2a}R^{2b}$, $C(O)NR^2R^{2a}$, $C(O)NR^2(CH_2)_rOR^2$, $SO_2NR^2R^{2a}$, $NR^2SO_2R^{2b}$, C_{3-6} carbocycle substituted with 0-2 R^{4a}, and 5-10 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1b} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

R^{1c} is selected from H, $CH(CH_2OR^2)_2$, $C(O)R^{2c}$, $C(O)NR^2R^{2a}$, $S(O)R^{2b}$, $S(O)_2R^{2b}$, and $SO_2NR^2R^{2a}$;

R^{1d} is selected from C_{3-13} carbocycle substituted with 0-2 R^{4a}, and 5-13 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1d} forms other than an N-N, N-S, or N-O bond;

R^2, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2a}, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, phenethyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2b}, at each occurrence, is selected from CF_3, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2c}, at each occurrence, is selected from CF_3, OH, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue

substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and comprising carbon atoms and from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3a}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3b}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3c}, at each occurrence, is selected from C_{1-4} alkyl, and phenyl;

R^{3d}, at each occurrence, is selected from H, C_{1-4} alkyl, C_{1-4} alkyl-phenyl, and $C(=O)R^{3c}$;

A is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^4, and 5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

X is selected from $-(CR^2R^{2a})_{1-4}-$, $-CR^2(CR^2R^{2b})(CH_2)_t-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-CR^2(OR^2)-$, $-CR^2(SR^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-SCR^2R^{2a}-$, $-S(O)CR^2R^{2a}-$, $-S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S-$, $-CR^2R^{2a}S(O)-$, $-CR^2R^{2a}S(O)_2-$, $-S(O)_2NR^2-$, $-NR^2S(O)_2-$, $-NR^2S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S(O)_2NR^2-$, $-NR^2S(O)_2NR^2-$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)O-$, $-OC(O)NR^2-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^{4a}, and

5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rN(\rightarrow O)R^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $(CH_2)_rNR^2C(O)R^{2b}$, $(CH_2)_rC(O)NR^2R^{2a}$, $(CH_2)_rNR^2C(O)NR^2R^{2a}$, $(CH_2)_rC(=NR^2)NR^2R^{2a}$, $(CH_2)_rC(=NS(O)_2R^5)NR^2R^{2a}$, $(CH_2)_rNHC(=NR^2)NR^2R^{2a}$, $(CH_2)_rC(O)NHC(=NR^2)NR^2R^{2a}$, $(CH_2)_rSO_2NR^2R^{2a}$, $(CH_2)_rNR^2SO_2NR^2R^{2a}$, $(CH_2)_rNR^2SO_2$-C_{1-4} alkyl, $(CH_2)_rNR^2SO_2R^5$, $(CH_2)_r-NR^2SO_2R^{5a}$, $(CH_2)_rS(O)_pR^5$, $(CH_2)_r-S(O)_pR^{5a}$, $(CF_2)_rCF_3$, $(CH_2)_r-CF_3$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-NR^{4e}R^{4f}$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-OR^{4e}$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-SR^{4e}$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-N(\rightarrow O)R^{4e}R^{4f}$, $(CH_2)_rNCH_2R^{1c}$,

$(CH_2)_rOCH_2R^{1c}$, $(CH_2)_rSCH_2R^{1c}$, $(CH_2)_rN(CH_2)_2(CH_2)_tR^{1b}$, $(CH_2)_rO(CH_2)_2(CH_2)_tR^{1b}$, $(CH_2)_rS(CH_2)_2(CH_2)_tR^{1b}$, $(CH_2)_r$5-6 membered carbocycle substituted with 0-1 R^5, and $(CH_2)_r$5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $C(=NS(O)_2R^5)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $C(O)NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, $(CF_2)_rCF_3$, $(CH_2)_r$-CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CF_2)_rCF_3$, $(CH_2)_r$-CF_3, $(CH_2)_r$-F, $(CH_2)_r$-Br, $(CH_2)_r$-Cl, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $(CH_2)_rN=CHOR^3$, $C(O)NH(CH_2)_2NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4b}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^3$, $(CH_2)_r$-F, $(CH_2)_r$-Cl, $(CH_2)_r$-Br, $(CH_2)_r$-I, C_{1-4} alkyl, $(CH_2)_r$-CN, $(CH_2)_r$-NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CH_2)_rCF_3$, and $(CF_2)_rCF_3$;

R^5, at each occurrence, is selected from H, C_{1-6} alkyl, =O, $(CH_2)_rOR^3$, F, Cl, Br, I, -CN, NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $CH(=NOR^{3d})$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CF_2)_rCF_3$, phenyl substituted with 0-2 R^6, naphthyl substituted with 0-2 R^6, and benzyl substituted with 0-2 R^6;

R^6, at each occurrence, is selected from H, OH, $(CH_2)_rOR^2$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2b}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $C(=NH)NH_2$, $NHC(=NH)NH_2$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, and $NR^2SO_2C_{1-4}$ alkyl;

R^7, at each occurrence, is selected from H, OH, C_{1-4} alkoxycarbonyl, C_{6-10} aryloxy, C_{6-10} aryloxycarbonyl, C_{6-10} arylmethylcarbonyl, C_{1-4} alkylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{6-10} arylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, phenylaminocarbonyl, and phenyl C_{1-4} alkoxycarbonyl;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

alternatively, R^7 and R^8, when attached to the same nitrogen, combine to form a 5-6 membered heterocyclic ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

R^9, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

n, at each occurrence, is selected from 0, 1, 2, and 3;

m, at each occurrence, is selected from 0, 1, and 2;

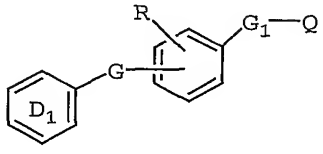
p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3;

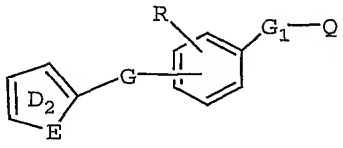
s, at each occurrence, is selected from 0, 1, and 2; and,

t, at each occurrence, is selected from 0, 1, 2, and 3.

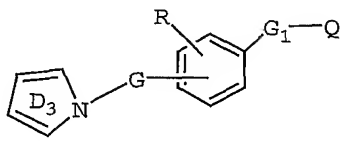
[2] In a preferred embodiment, the present invention provides a novel compound, wherein the compound is of formula Ia_1-Ic_1, wherein:



Ia_1



Ib_1



Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E

is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

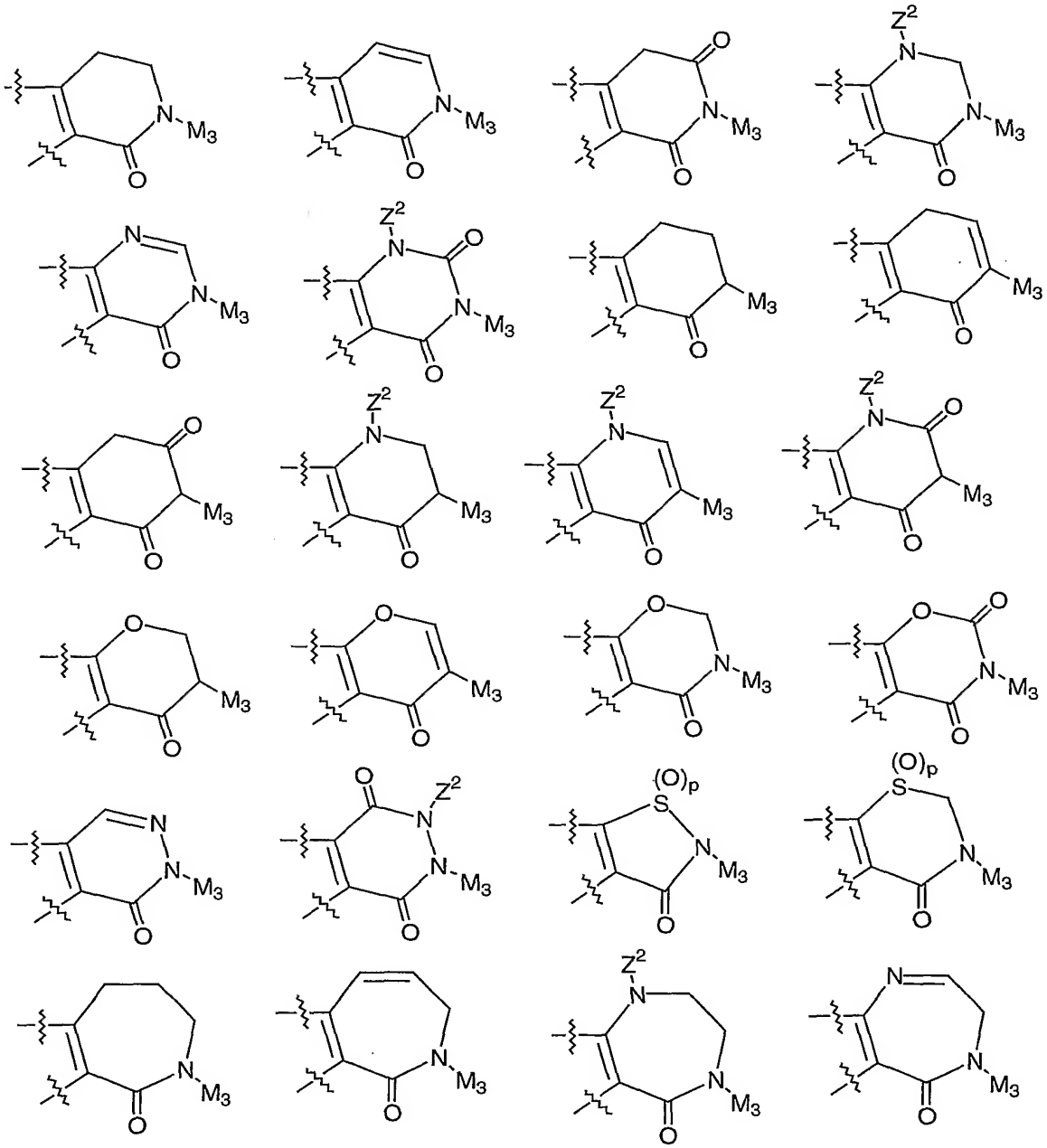
R^a is selected from H, OH, SH, C_{1-3} alkoxy, C_{1-3} thioalkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

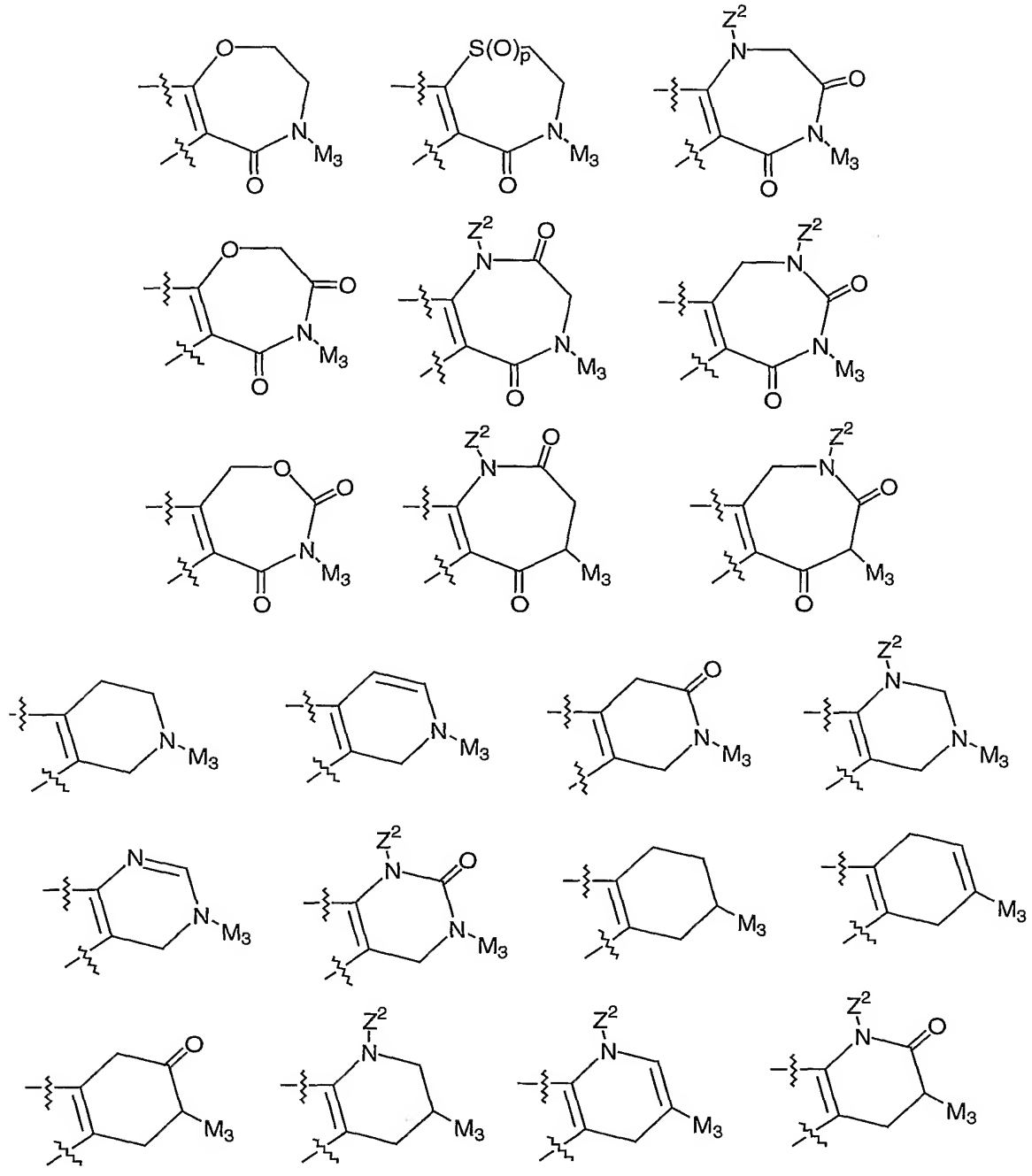
R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

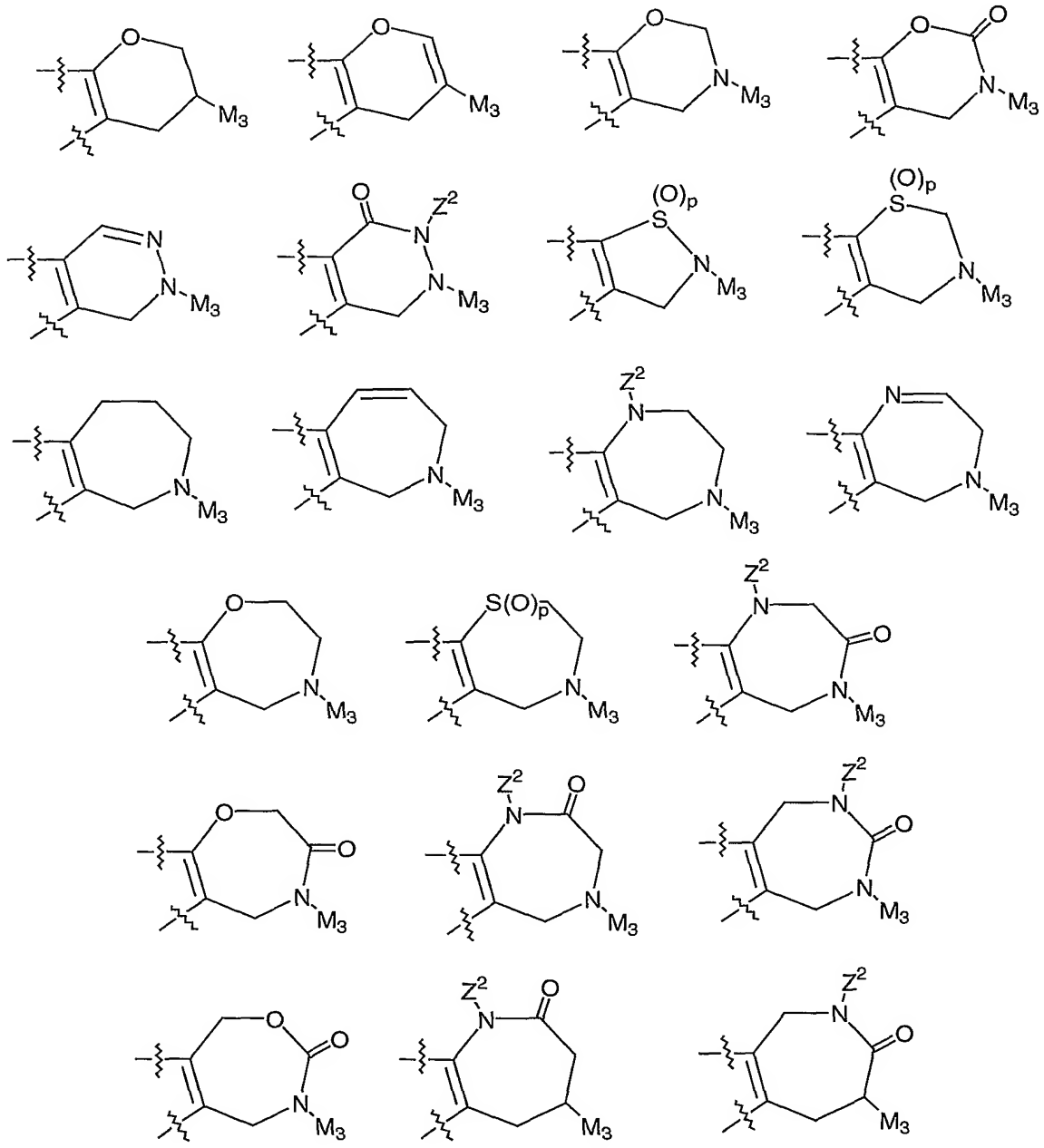
R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

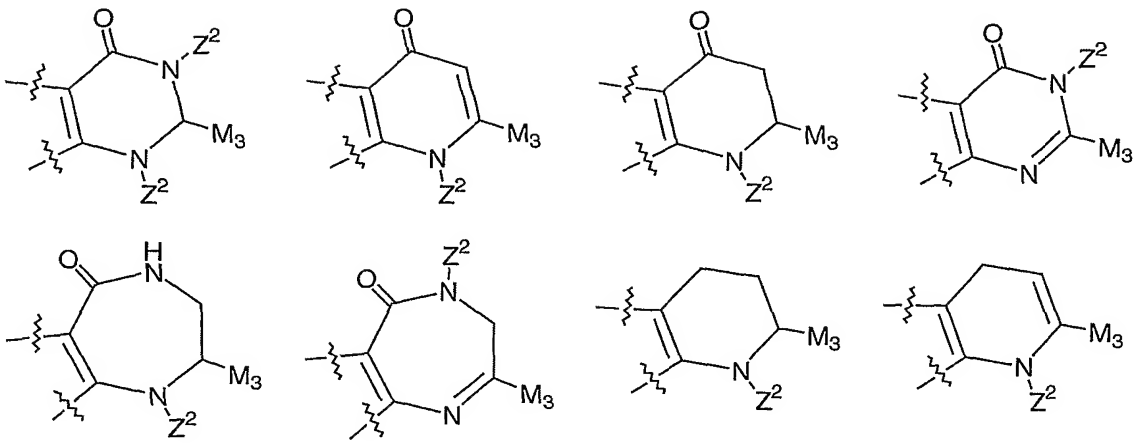
G_1 is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$, and provided that G_1-Q form other than a N-N, O-N, or S-N bond;

ring M is substituted with 0-2 R^{1a} and is selected from the group:



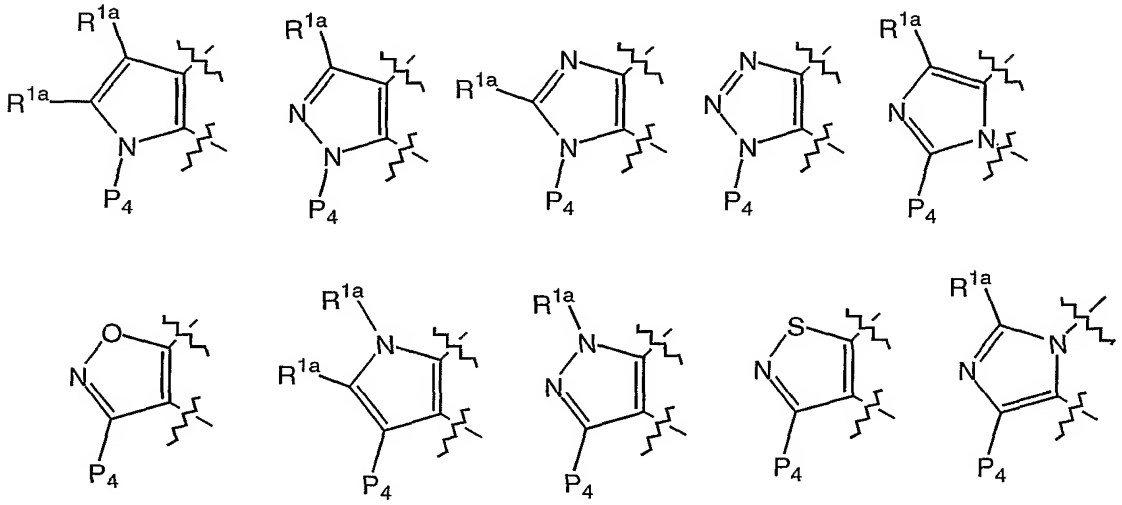






Z^2 is selected from H, C_{1-4} alkyl, phenyl, benzyl, $C(O)R^3$, and $S(O)_pR^{3c}$;

ring P, including P_1, P_2, P_3, and P_4 is selected from group:



G_1 is absent or is selected from $(CR^3R^{3a})_{1-3}$, $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uO(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)NR^3(CR^3R^{3a})_w$, and $(CR^3R^{3a})_uS(O)_2NR^3(CR^3R^{3a})_w$, wherein u + w total 0, 1, or 2, provided that G_1 does

not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

A is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^4;

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

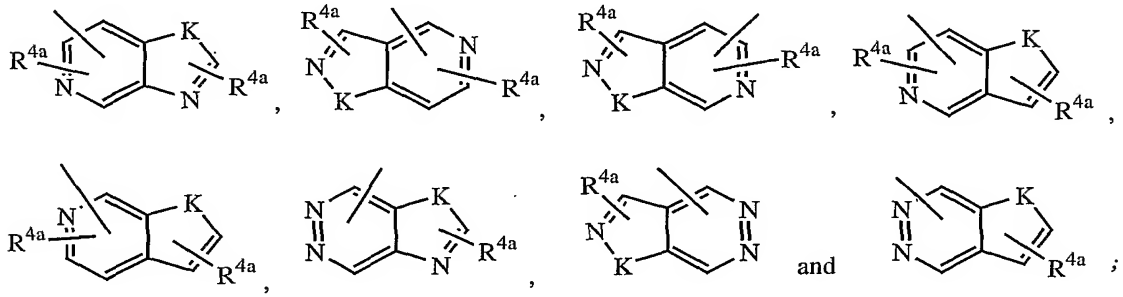
X is selected from $-(CR^2R^{2a})_{1-4}-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^{4a};

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,

1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic heteroaryl ring systems:



and ;

K is selected from O, S, NH, and N;

Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, $C(O)NH$, $NHC(O)$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

[3] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_1 or Ic_1, wherein;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

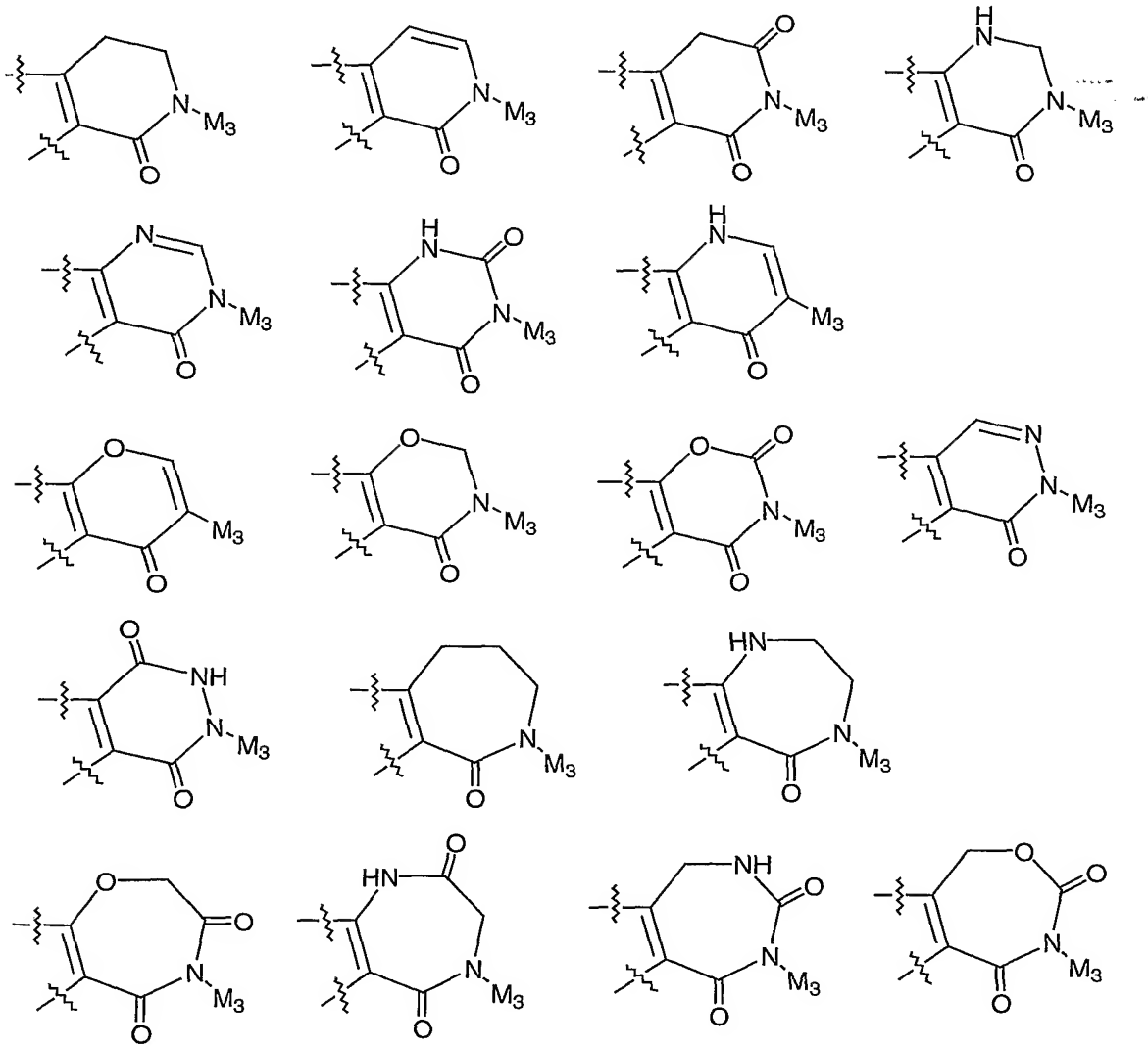
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

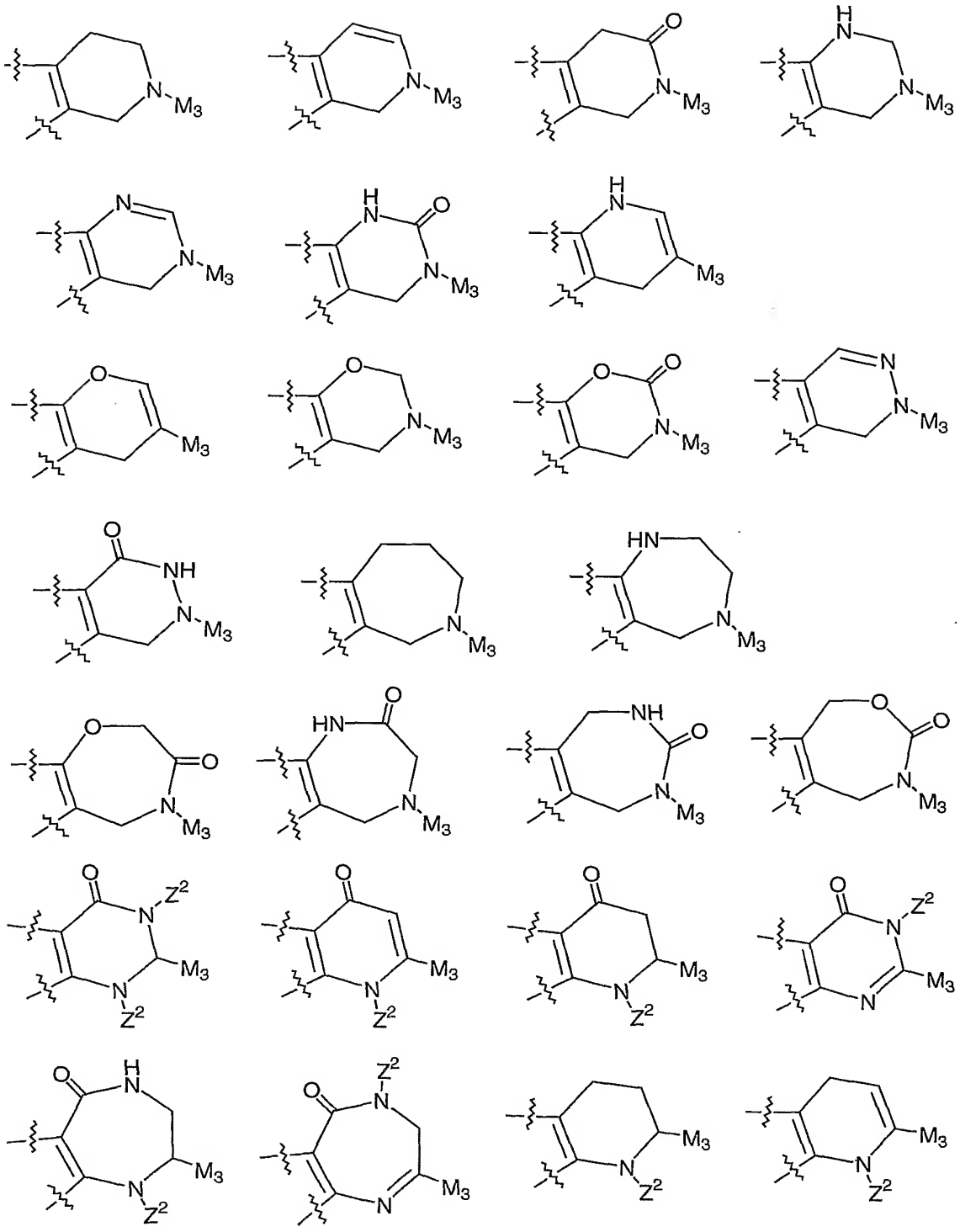
R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

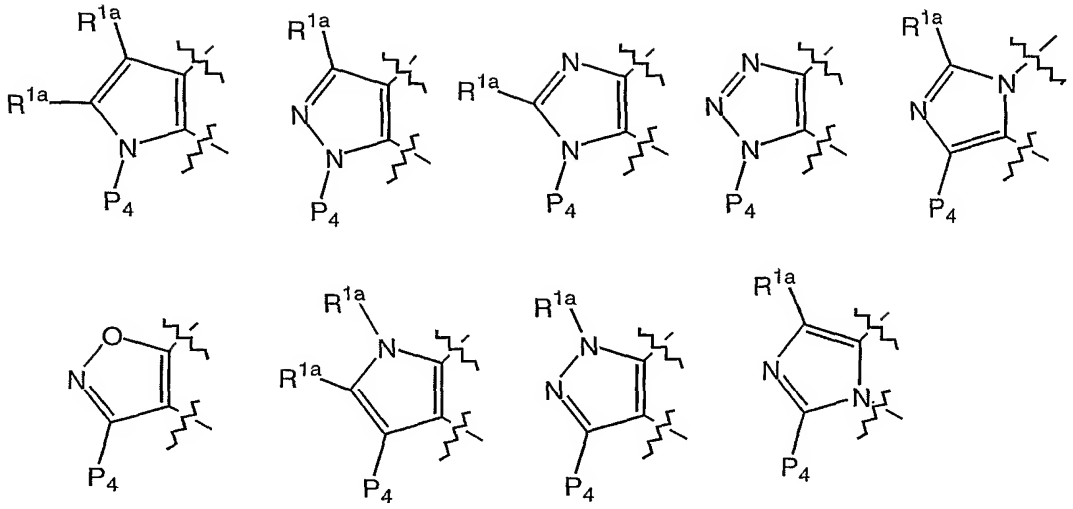
R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl$)_2$;

ring M is substituted with 0-2 R^{1a} and is selected from the group:





ring P, including P_1, P_2, P_3, and P_4 is selected from group:



Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran, benzothiofuran, indole, benzimidazole, benzimidazolone, benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole;

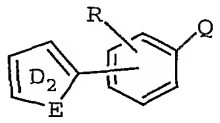
Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, C(O)NH, NHC(O), $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$,

$NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

[4] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_2:



Ib_2

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

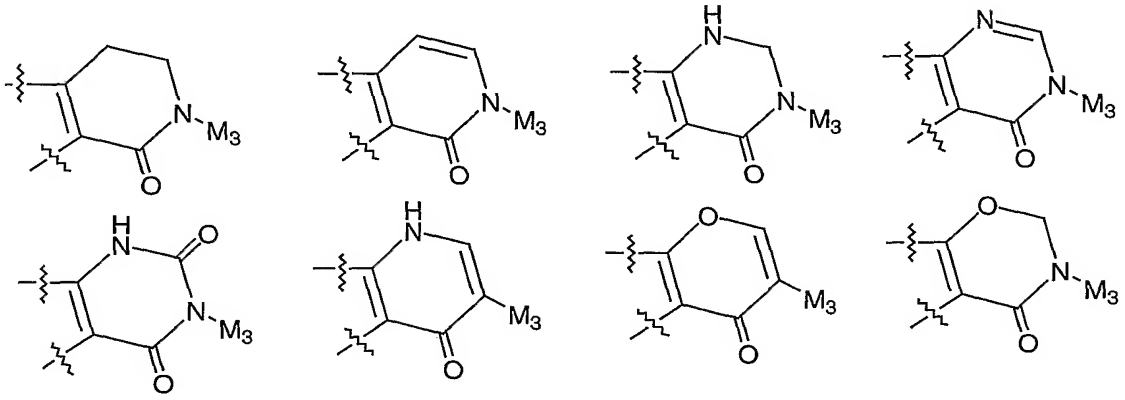
ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N- R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

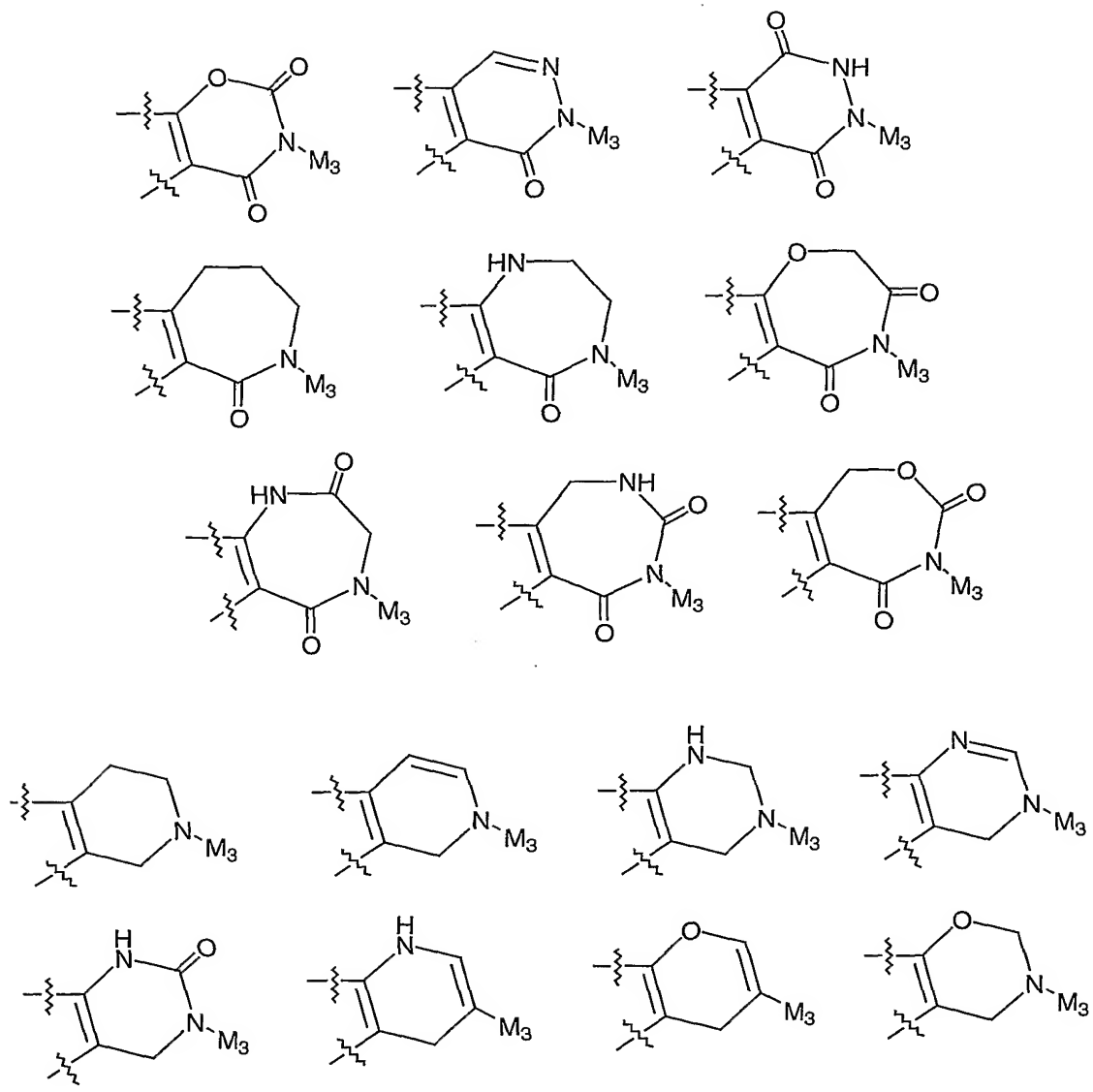
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

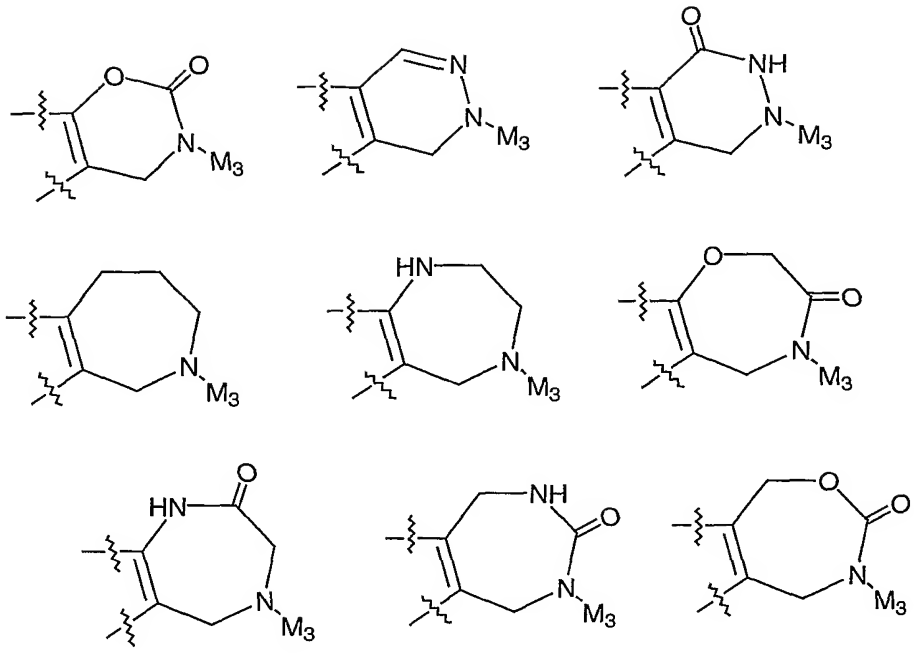
R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), and $N(C_{1-3}$ alkyl)$_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

ring M is substituted with 0-1 R^{1a} and is selected from the group:

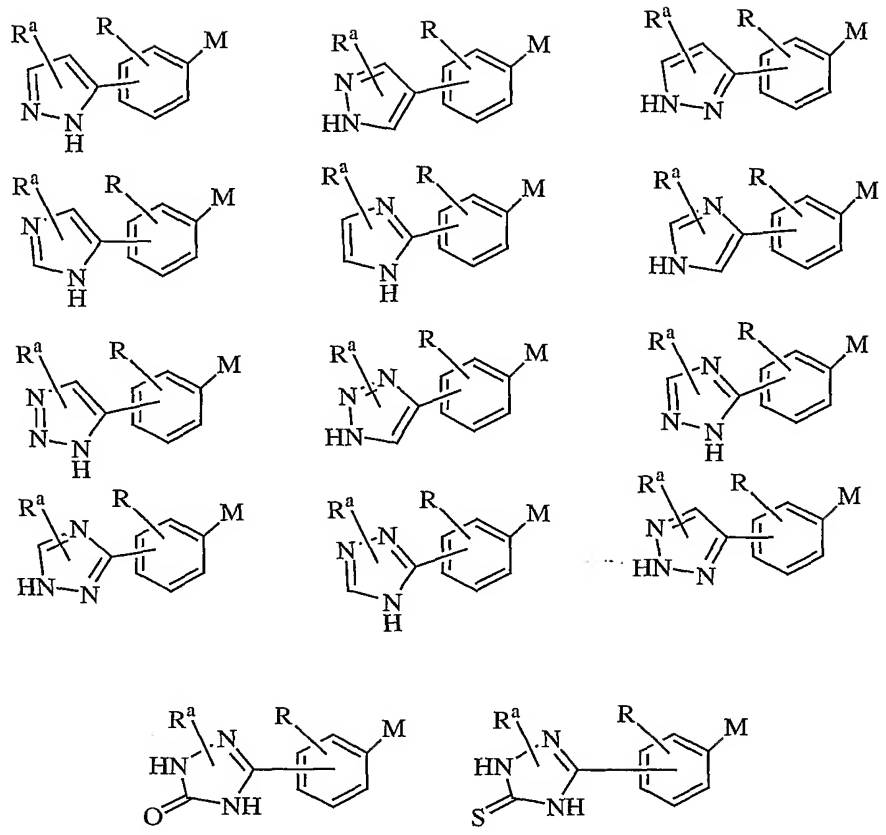






G_1 is absent or is selected from CH_2, CH_2CH_2, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, $C(O)NH$, $NHC(O)$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached.

[5] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is selected for one of the formulas:



or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

G_1 is absent;

A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R^4; and,

B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R^{4a};

R^2, at each occurrence, is selected from H, CH_3, CH_2CH_3, cyclopropylmethyl, cyclobutyl, and cyclopentyl;

R^{2a}, at each occurrence, is selected from H, CH_3, and CH_2CH_3;

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form pyrrolidine substituted with 0-2 R^{4b} or piperidine substituted with 0-2 R^{4b};

R^4, at each occurrence, is selected from OH, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, F, Br, Cl, I, C_{1-4} alkyl, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, CF_3, and $(CF_2)CF_3$;

R^{4a} is selected from C_{1-4} alkyl, CF_3, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, SR^5, $S(O)R^5$, $S(O)_2R^5$, $SO_2NR^2R^{2a}$, and 1-CF_3-tetrazol-2-yl;

R^{4b}, at each occurrence, is selected from H, CH_3, and OH;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl; and,

r, at each occurrence, is selected from 0, 1, and 2.

[6] In another preferred embodiment, the present invention provides a novel compound, wherein;

A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl; and,

B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-

dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

[7] In another preferred embodiment, the present invention provides a novel compound selected from the group:

1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-methyl-6-[2'-aminosulfonyl-[1,1']-biphen-4-yl]-1,4,5,6-tetrahydropyrazolo-[3,4-*c*]-pyridin-7-one trifluoroacetic acid salt;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-

pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-

fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

or a pharmaceutically acceptable salt thereof.

[8] In another preferred embodiment, the present invention provides a novel compound selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-

biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-

biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

or a pharmaceutically acceptable salt thereof.

[9] In another preferred embodiment, the present invention provides a novel compound selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-

biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

or a pharmaceutically acceptable salt thereof.

[10] In another preferred embodiment, the present invention provides a novel compound selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-

fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-

fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

or a pharmaceutically acceptable salt thereof.

[11] In another preferred embodiment, the present invention provides a novel compound selected from the group:

1-[3-(5-oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-(2'-{[(3*S*)-3-Hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-{2'-[(Dimethylamino)methyl]-1,1'-biphenyl-4-yl}-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-[2'-(Methylsulfonyl)-1,1'-biphenyl-4-yl]-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-6-{2'-[(dimethylamino)methyl]-1,1'-biphenyl-4-yl}-3-

(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-{2'-[(dimethylamino)methyl]-1,1'-biphenyl-4-yl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-(4-{2-[(dimethylamino)methyl]-1*H*-imidazol-1-yl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-{4-[2-(1-pyrrolidinylmethyl)-1*H*-imidazol-1-yl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-(4-{2-[(Dimethylamino)methyl]-1*H*-imidazol-1-yl}phenyl)-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

3-Methyl-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-{4-[2-(1-pyrrolidinylmethyl)-1*H*-imidazol-1-yl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

7-Oxo-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-

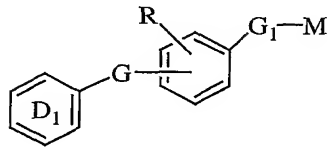
4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-[3-(5-Oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-7-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[3,4-*c*]azepin-8(1*H*)-one; and,

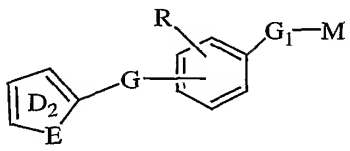
1-[2-(5-Oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

or a pharmaceutically acceptable salt thereof.

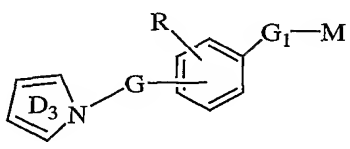
In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ia_1-Ic_1, wherein:



Ia_1



Ib_1



Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^a is selected from H, OH, SH, C_{1-3} alkoxy, C_{1-3} thioalkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$;

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl$)_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl$)_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl$)_2$; and,

G_1 is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$, and provided that G_1-M form other than a N-N, O-N, or S-N bond.

In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_1 or Ic_1, wherein;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

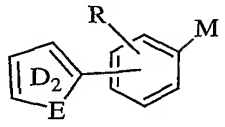
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$; and,

R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$.

In another embodiment, the present invention provides a novel compound, wherein the compound is of formula Ib_2:



Ib_2

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E

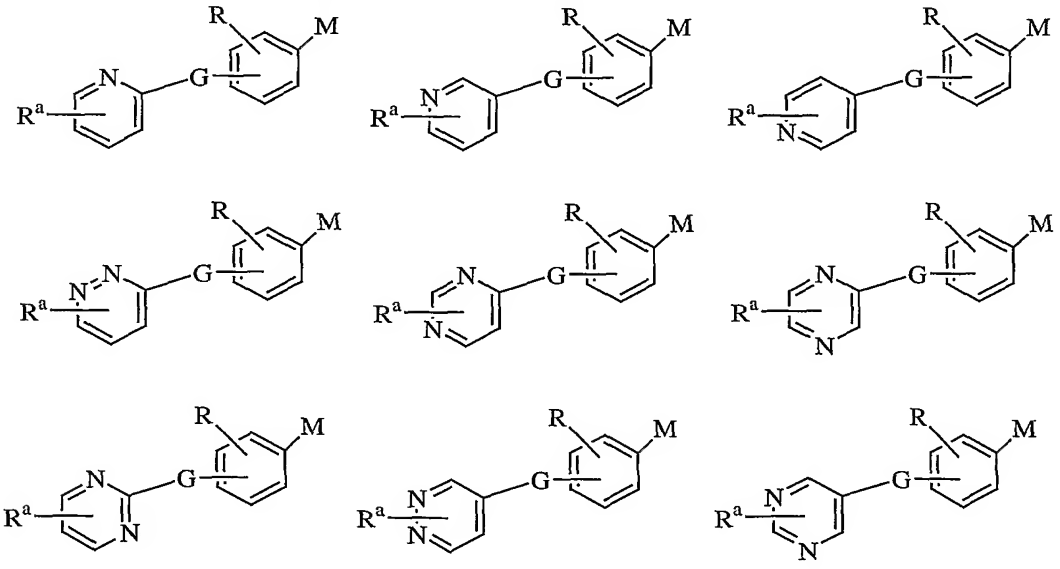
is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

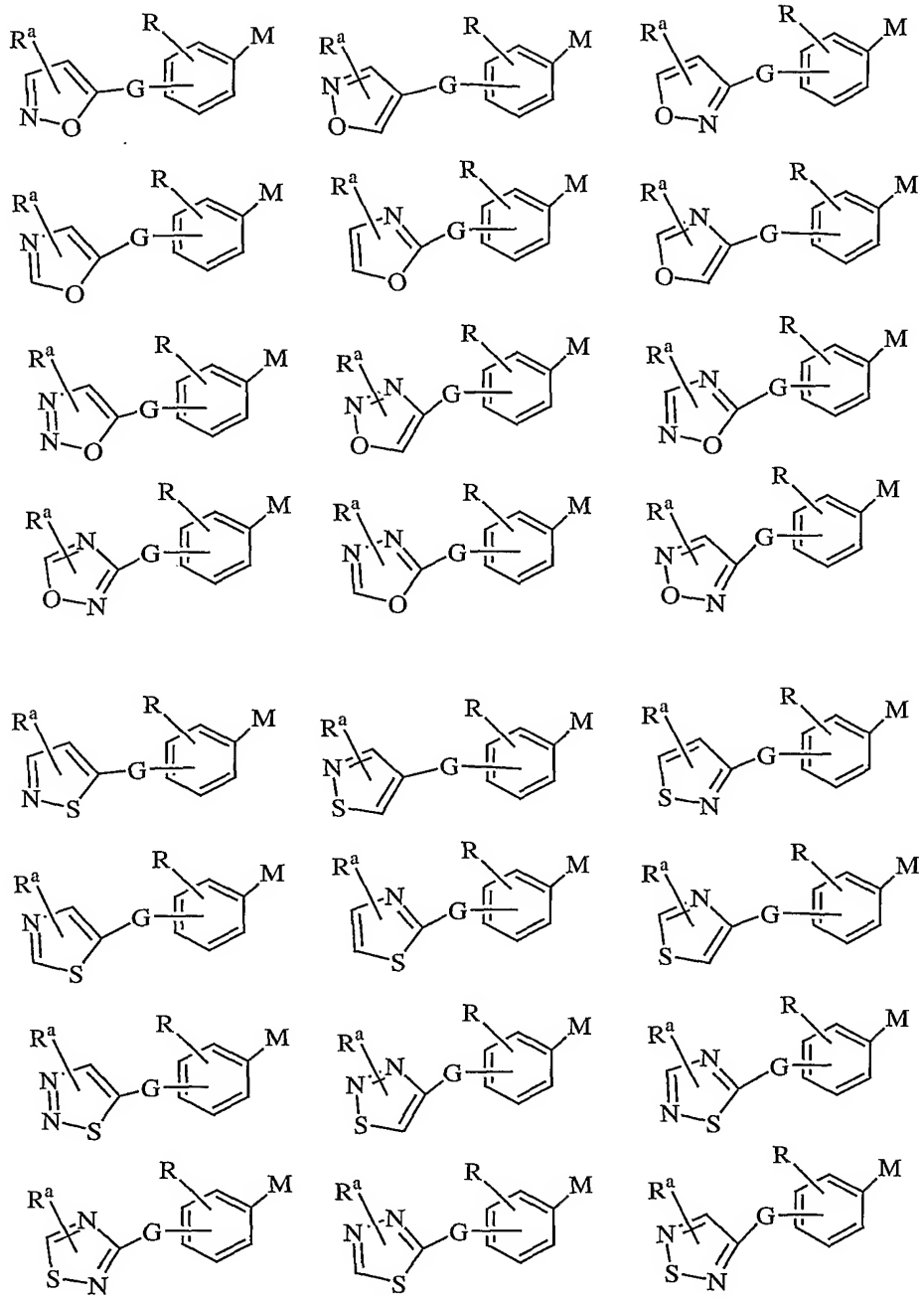
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

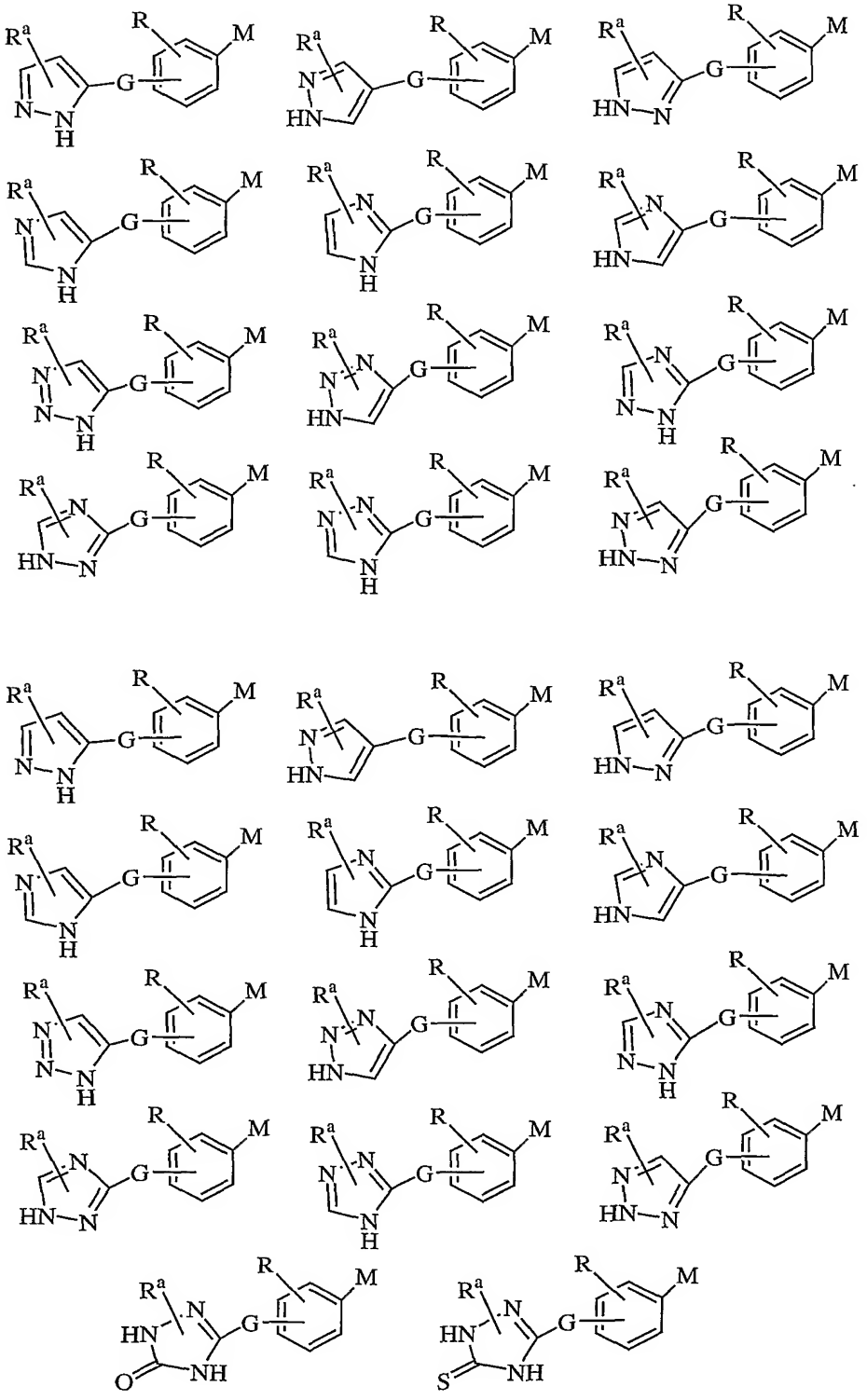
R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), and $N(C_{1-3}$ alkyl)$_2$; and,

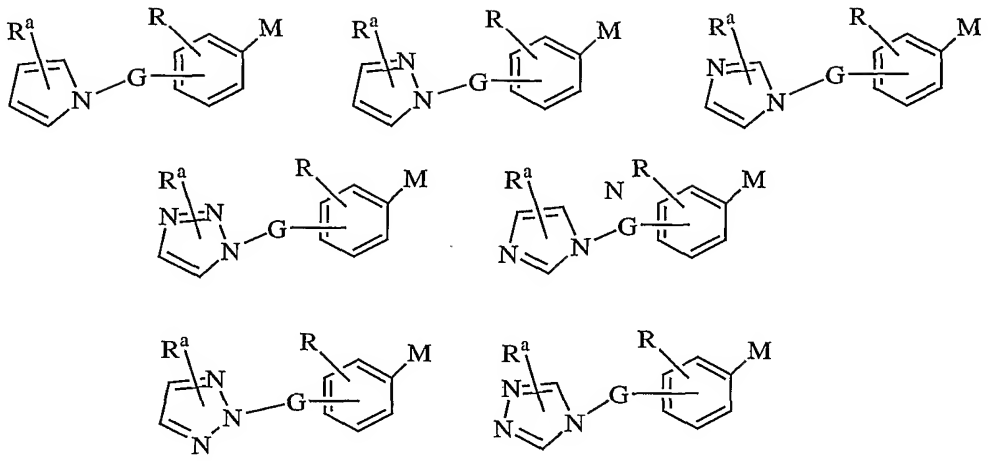
R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$.

In another embodiment, the present invention provides a novel compound selected from one of the formulas:



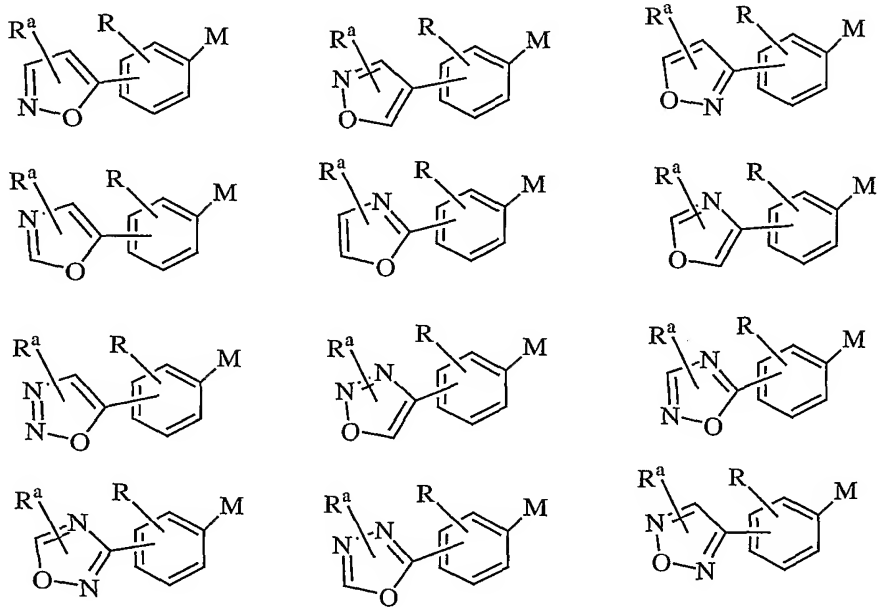


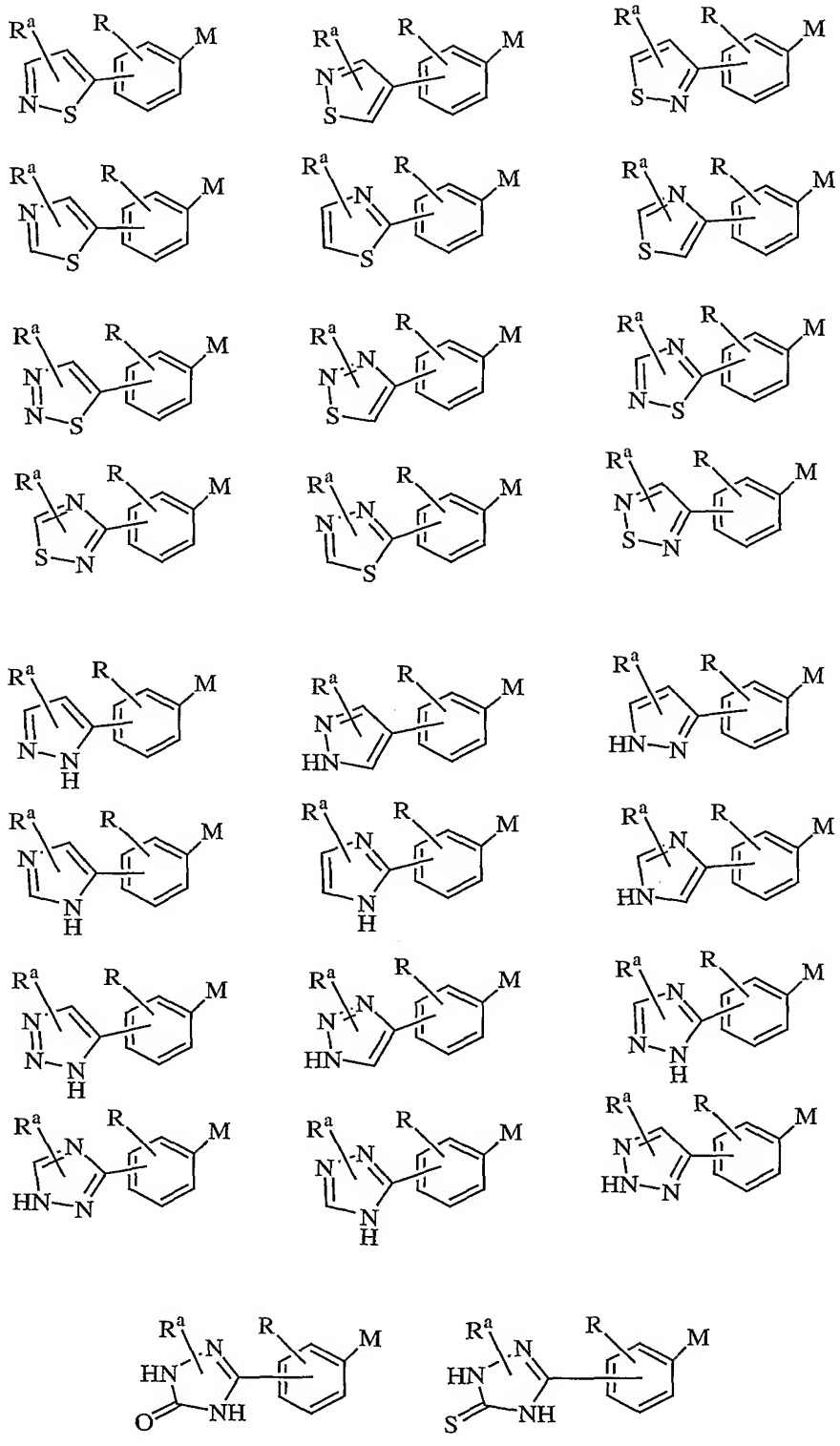




or a stereoisomer or pharmaceutically acceptable salt thereof.

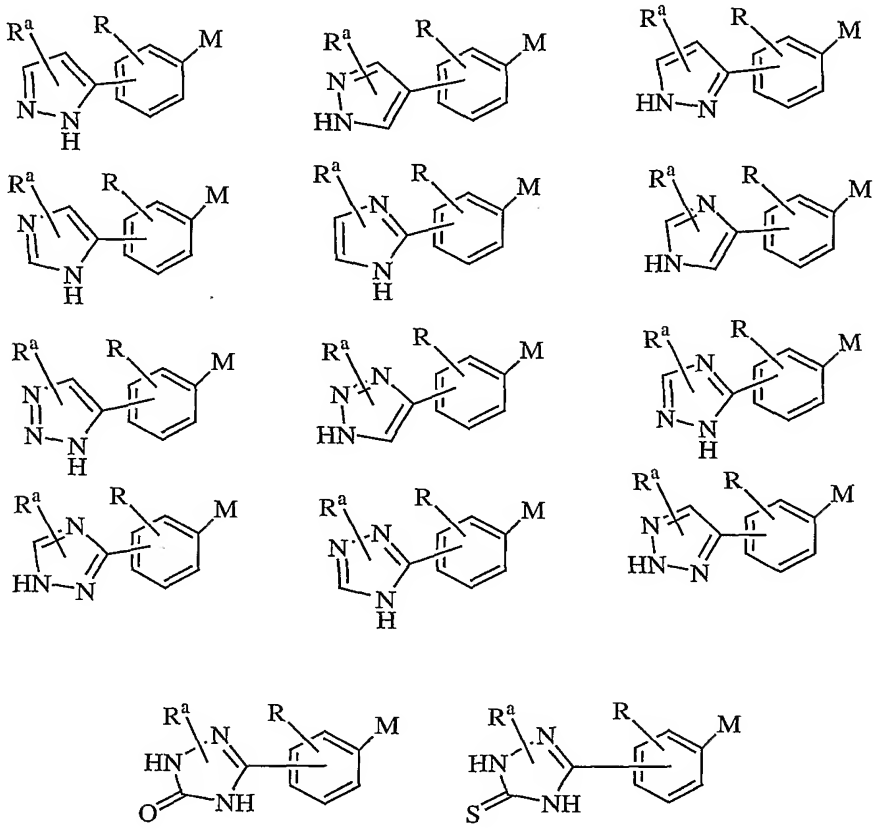
In another embodiment, the present invention provides a novel compound selected from one of the formulas:





or a stereoisomer or pharmaceutically acceptable salt thereof.

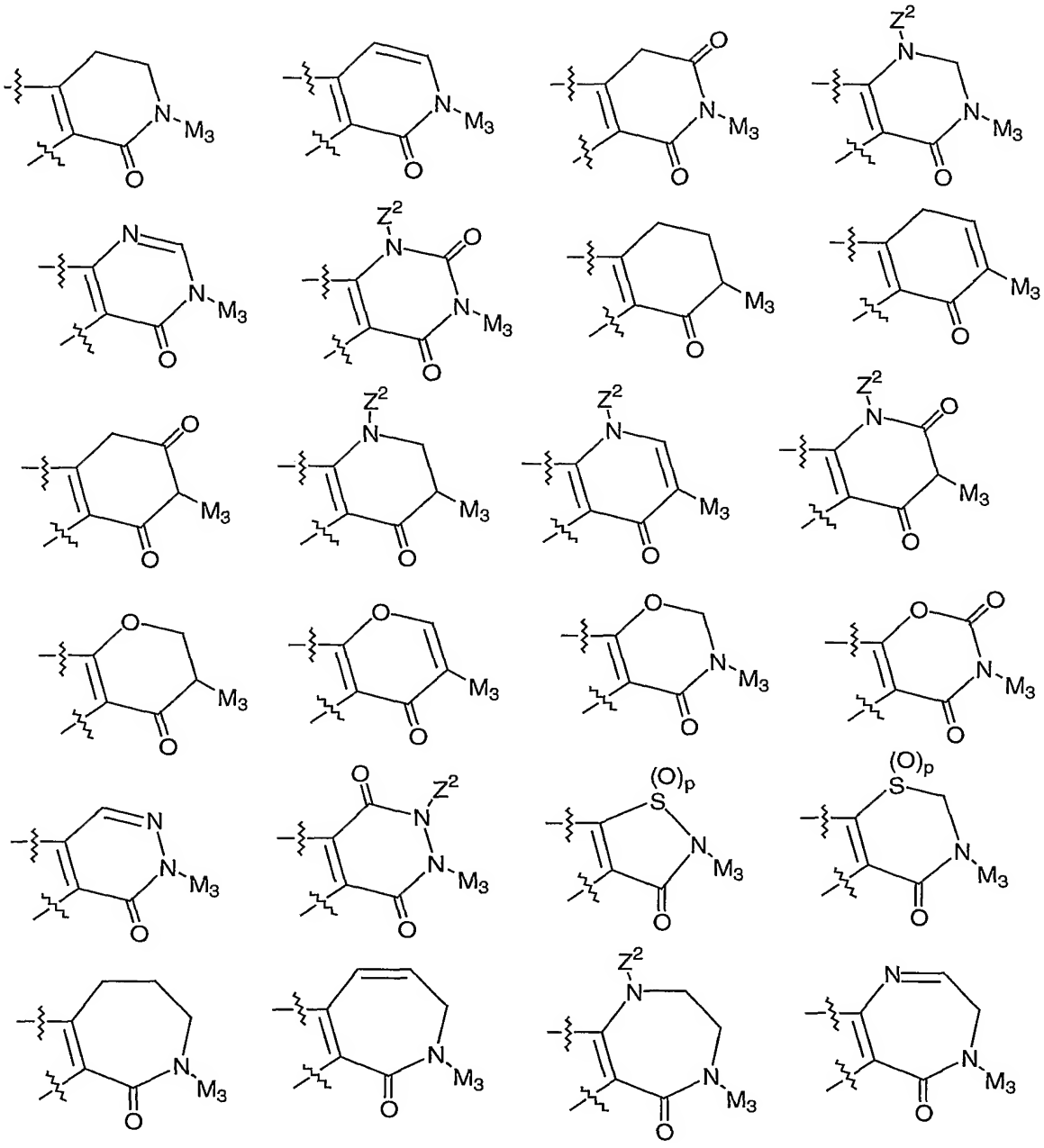
In another embodiment, the present invention provides a novel compound selected from one of the formulas:

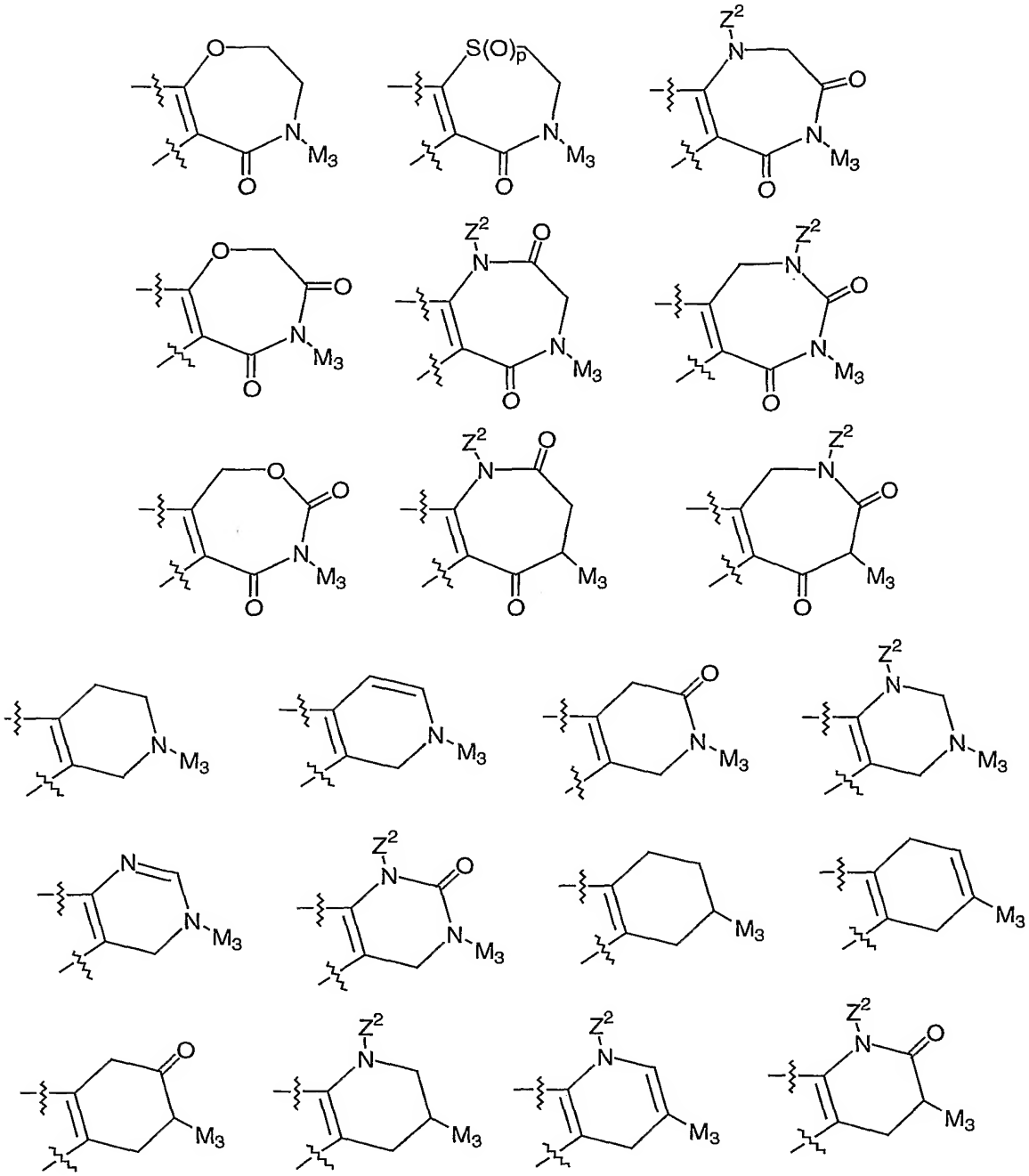


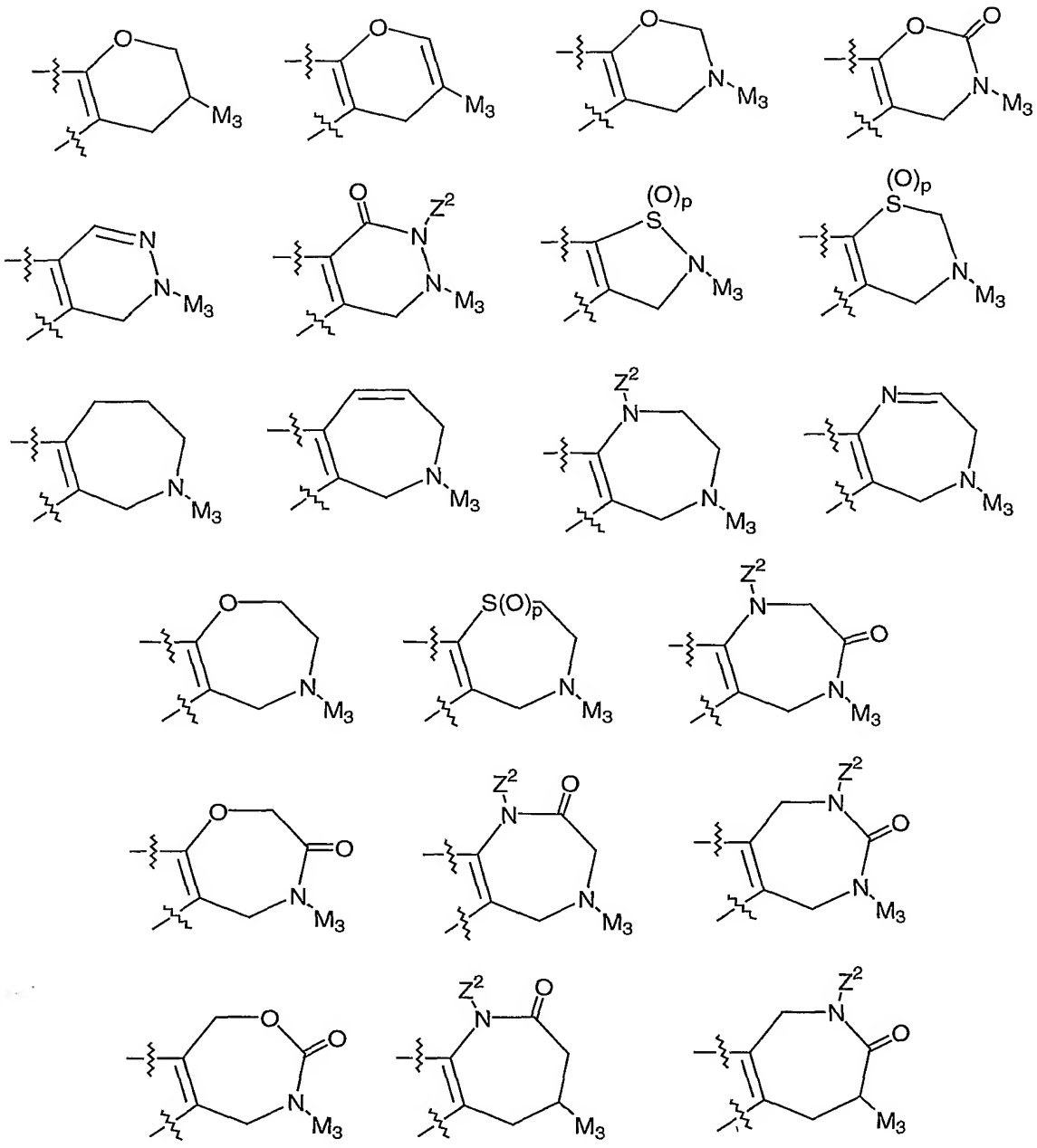
or a stereoisomer or pharmaceutically acceptable salt thereof.

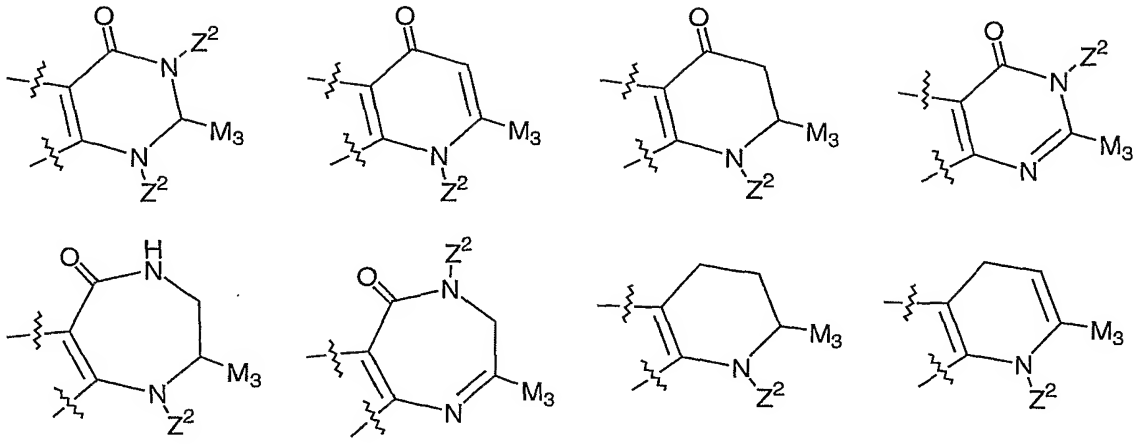
In another embodiment, the present invention provides a novel compound wherein:

ring M is substituted with 0-2 R^{1a} and is selected from the group:



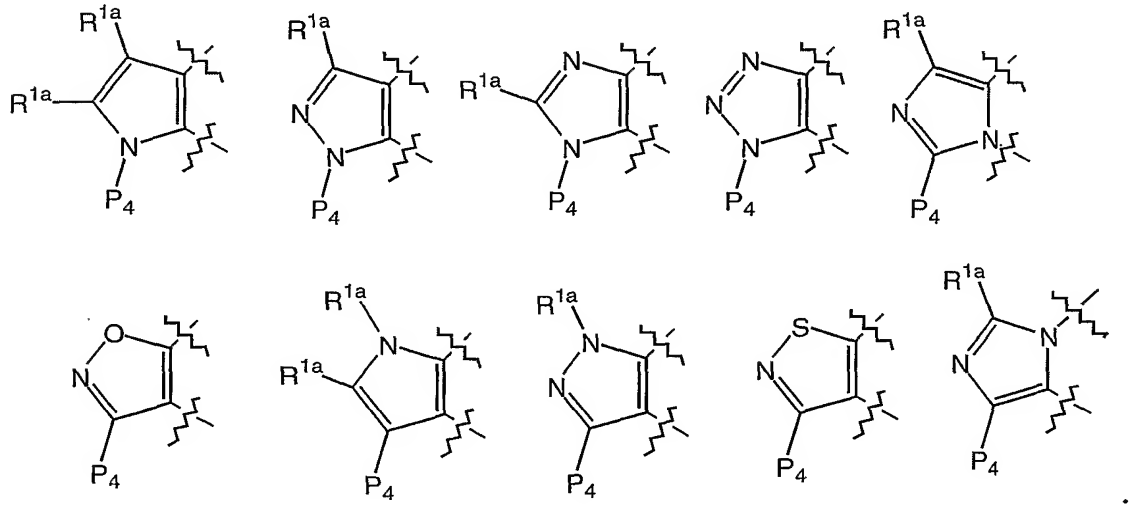






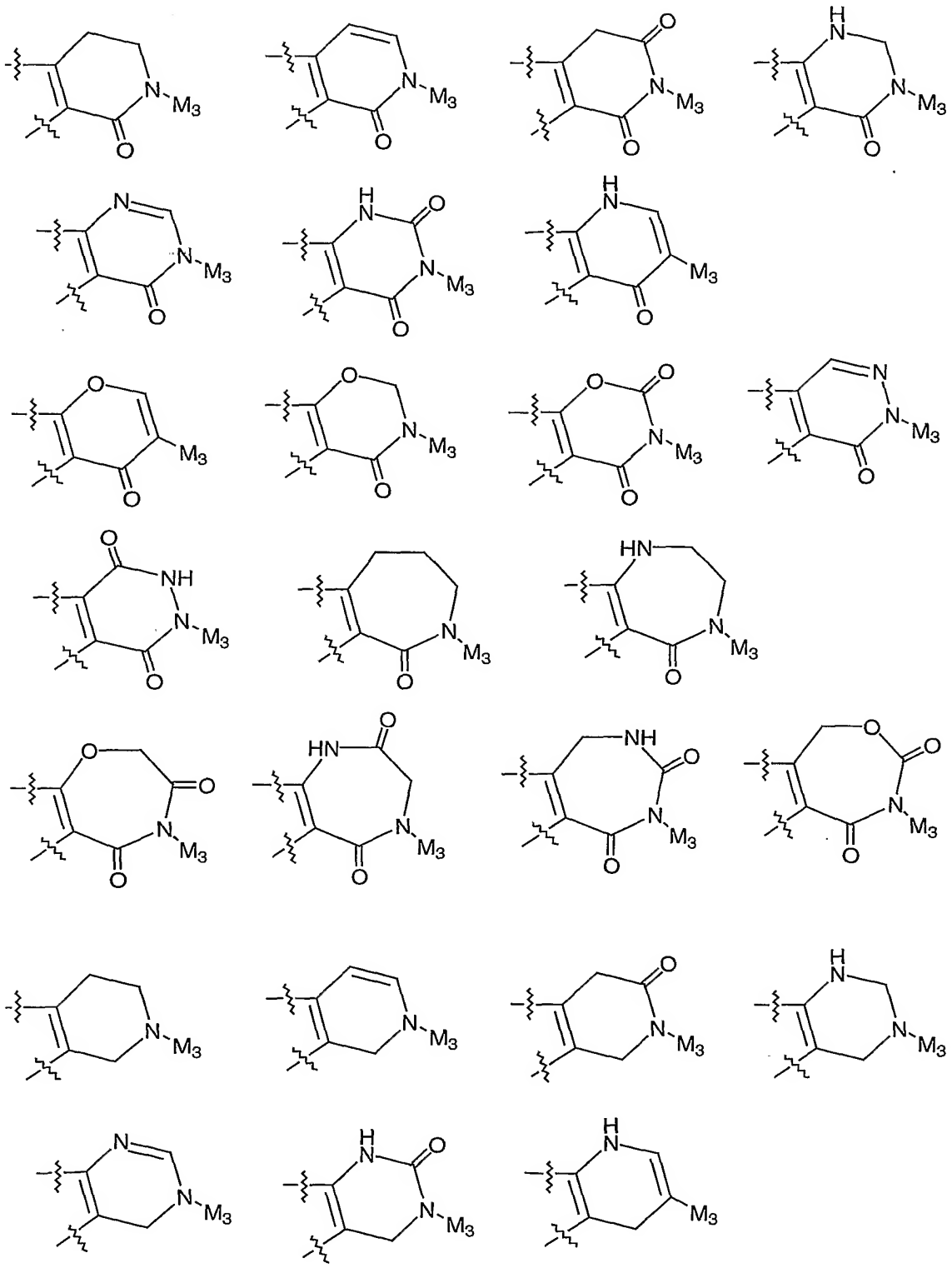
Z^2 is selected from H, C_{1-4} alkyl, phenyl, benzyl, $C(O)R^3$, and $S(O)_pR^{3c}$;

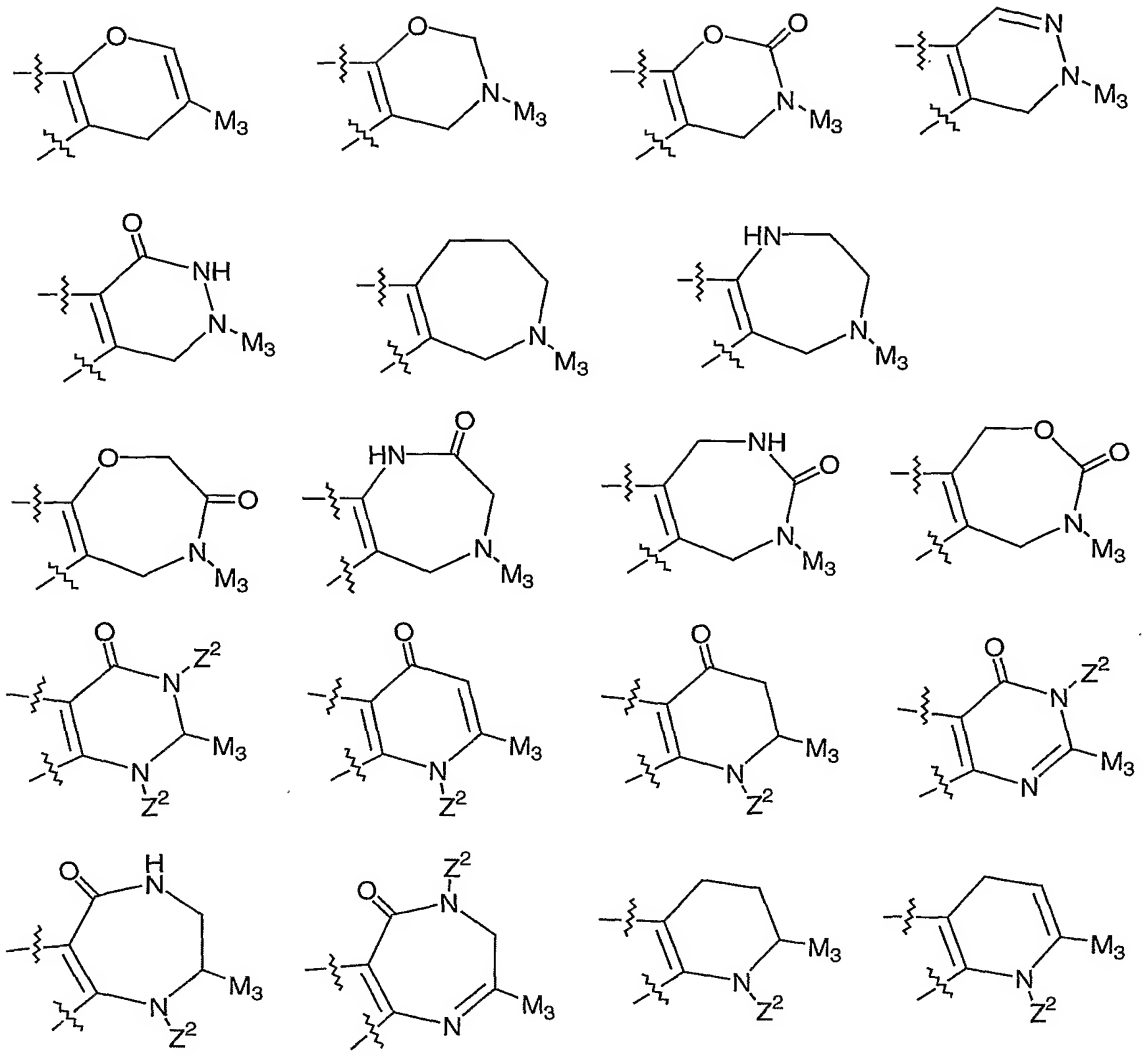
ring P, including P_1, P_2, P_3, and P_4 is selected from group:



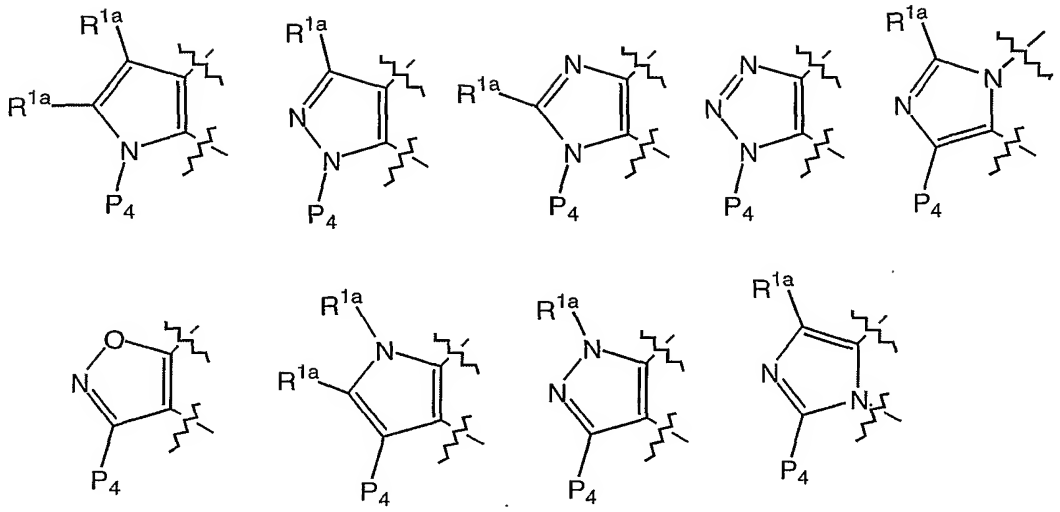
In another embodiment, the present invention provides a novel compound wherein:

ring M is substituted with 0-2 R^{1a} and is selected from the group:



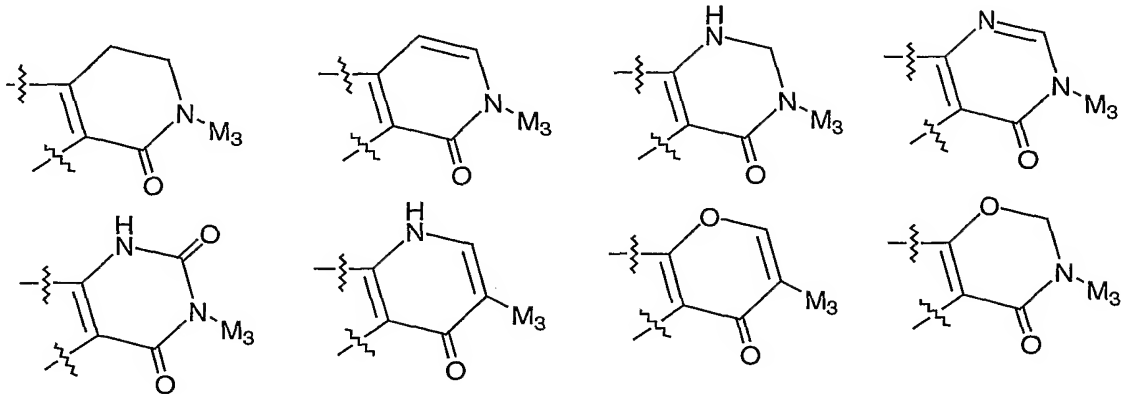


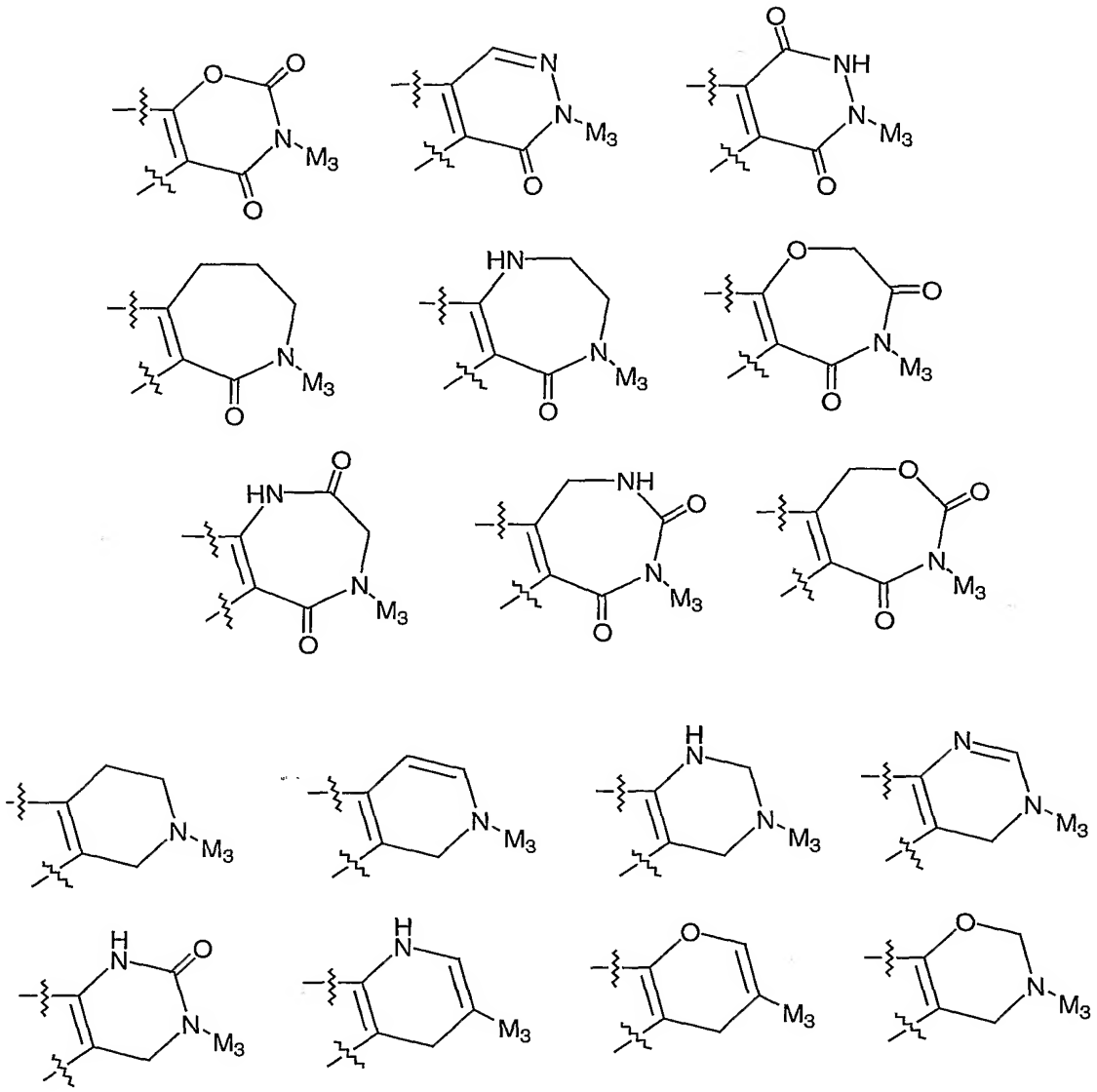
ring P, including P_1, P_2, P_3, and P_4 is selected from group:

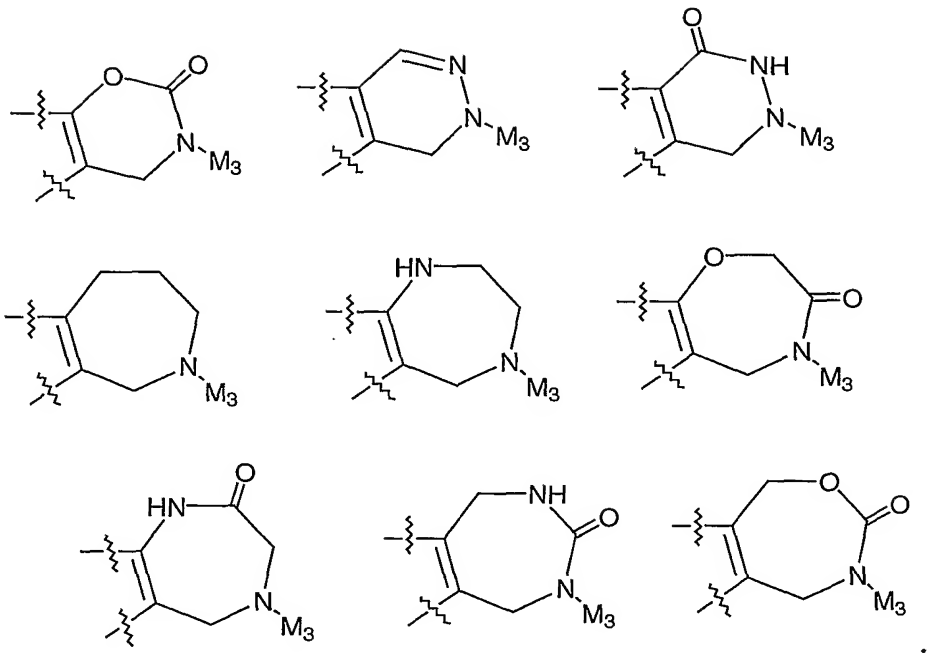


In another embodiment, the present invention provides a novel compound wherein:

ring M is substituted with 0-1 R^{1a} and is selected from the group:







In another embodiment, the present invention provides a novel compound wherein A is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^4;

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

In another embodiment, the present invention provides a novel compound wherein A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R^4.

In another embodiment, the present invention provides a novel compound wherein A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl.

In another embodiment, the present invention provides a novel compound wherein:

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

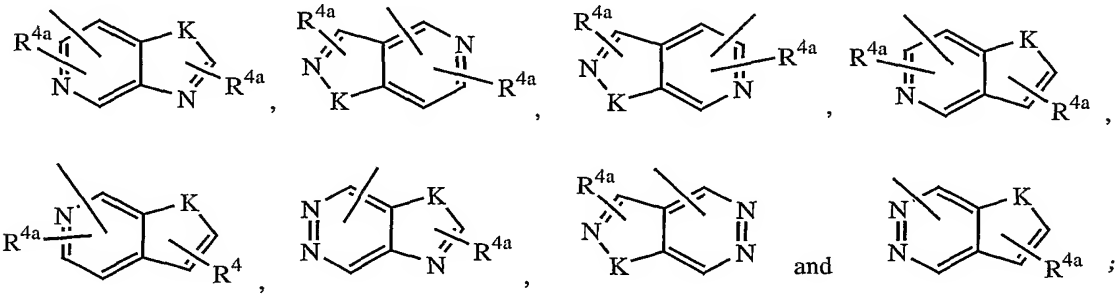
X is selected from $-(CR^2R^{2a})_{1-4}-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^{4a};

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,

1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic heteroaryl ring systems:



and ;

K is selected from O, S, NH, and N.

In another embodiment, the present invention provides a novel compound wherein:

Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran, benzothiofuran, indole, benzimidazole, benzimidazolone,

benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole.

In another embodiment, the present invention provides a novel compound wherein B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R^{4a}.

In another embodiment, the present invention provides a novel compound wherein B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

In another embodiment, the present invention provides novel pharmaceutical compositions, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula Ia, Ib, or Ic or a pharmaceutically acceptable salt form thereof.

In another embodiment, the present invention provides a novel method for treating or preventing a thromboembolic disorder, comprising: administering to a patient in need thereof a therapeutically effective amount of a compound of formula Ia, Ib, or Ic or a pharmaceutically acceptable salt form thereof.

In another embodiment, the present invention provides a compound of formula Ia, Ib, or Ic as described above for use in therapy.

In another embodiment, the present invention provides the use of a compound formula Ia, Ib, or Ic as described above for the manufacture of a medicament for the treatment of a thromboembolic disorder.

DEFINITIONS

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated. All processes

used to prepare compounds of the present invention and intermediates made therein are considered to be part of the present invention. All tautomers of shown or described compounds are also considered to be part of the present invention.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced. Keto substituents are not present on aromatic moieties.

The present invention is intended to include all isotopes of atoms occurring in the present compounds. Isotopes include those atoms having the same atomic number but different mass numbers. By way of general example and without limitation, isotopes of hydrogen include tritium and deuterium. Isotopes of carbon include C-13 and C-14.

When any variable (e.g., R^6) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 R^6, then said group may optionally be substituted with up to two R^6 groups and R^6 at each occurrence is selected independently from the definition of R^6. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such

substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein, "alkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms. C_{1-6} alkyl, is intended to include C_1, C_2, C_3, C_4, C_5, and C_6 alkyl groups. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, and s-pentyl. "Haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example $-C_vF_w$ where v = 1 to 3 and w = 1 to (2v+1)). Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, and pentachloroethyl. "Alkoxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. C_{1-6} alkoxy, is intended to include C_1, C_2, C_3, C_4, C_5, and C_6 alkoxy groups. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. "Cycloalkyl" is intended to include saturated ring groups, such as cyclopropyl, cyclobutyl, or cyclopentyl. C_{3-7} cycloalkyl is intended to include C_3, C_4, C_5, C_6, and C_7 cycloalkyl groups. Alkenyl" is intended to include hydrocarbon chains of either straight or branched configuration and one or more unsaturated carbon-carbon bonds that may occur in any stable point along the chain, such as ethenyl and propenyl. C_{2-6} alkenyl is intended to include C_2, C_3, C_4, C_5, and C_6 alkenyl groups. "Alkynyl" is intended to include hydrocarbon chains of either straight or branched configuration and one or more triple carbon-carbon bonds that may occur in any stable point along the chain,

such as ethynyl and propynyl. C_{2-6} Alkynyl is intended to include C_2, C_3, C_4, C_5, and C_6 alkynyl groups.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo; and "counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, and sulfate.

As used herein, "carbocycle" or "carbocyclic residue" is intended to mean any stable 3, 4, 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, 10, 11, 12, or 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane, [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, and tetrahydronaphthyl.

As used herein, the term "heterocycle" or "heterocyclic system" is intended to mean a stable 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, or 10-membered bicyclic heterocyclic ring which is saturated, partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, NH, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. A nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. It

is preferred that the total number of S and O atoms in the heterocycle is not more than 1. As used herein, the term "aromatic heterocyclic system" or "heteroaryl" is intended to mean a stable 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, or 10-membered bicyclic heterocyclic aromatic ring which consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, NH, O and S. It is to be noted that total number of S and O atoms in the aromatic heterocycle is not more than 1.

Examples of heterocycles include, but are not limited to, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzoxazolinyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolinyl, carbazolyl, 4a*H*-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isatinoyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxindolyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl,

tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, and xanthenyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-

acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound that contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, non-aqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (e.g., solubility, bioavailability, manufacturing, etc...) the compounds of the present invention may be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same and compositions containing the same. "Prodrugs" are intended to include any covalently bonded carriers that release an active parent drug of the present invention *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug of the present invention is administered to a mammalian subject, it cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not

limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of the present invention.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

"Substituted" is intended to indicate that one or more hydrogens on the atom indicated in the expression using "substituted" is replaced with a selection from the indicated group(s), provided that the indicated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O) group, then 2 hydrogens on the atom are replaced.

"Therapeutically effective amount" is intended to include an amount of a compound of the present invention or an amount of the combination of compounds claimed effective to inhibit factor Xa. The combination of compounds is preferably a synergistic combination. Synergy, as described, for example, by Chou and Talalay, *Adv. Enzyme Regul.* **1984**, *22*:27-55, occurs when the effect (in this case, inhibition of factor Xa) of the compounds when administered in combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at sub-optimal concentrations of the compounds. Synergy can be in terms of lower cytotoxicity, increased antiviral effect, or some other beneficial effect of the combination compared with the individual components.

SYNTHESIS

The compounds of the present invention can be prepared in a number of ways known to one skilled in the art of organic synthesis. The compounds of the present invention

can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or by variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those described below. The reactions are performed in a solvent appropriate to the reagents and materials employed and suitable for the transformations being effected. It will be understood by those skilled in the art of organic synthesis that the functionality present on the molecule should be consistent with the transformations proposed. This will sometimes require a judgment to modify the order of the synthetic steps or to select one particular process scheme over another in order to obtain a desired compound of the invention. It will also be recognized that another major consideration in the planning of any synthetic route in this field is the judicious choice of the protecting group used for protection of the reactive functional groups present in the compounds described in this invention. An authoritative account describing the many alternatives to the trained practitioner is Greene and Wuts (*Protective Groups In Organic Synthesis*, Wiley and Sons, **1991**). All references cited herein are hereby incorporated in their entirety herein by reference.

The compounds of the present invention represented by Formulas Ia, Ib, and Ic consist of a group "Ring D-G-G^2-G^1" (i.e., P_4 or M_3) and a group "Z-A-B" (i.e., the remaining of P_4 or M_3) attached to a [5,6]- or [5,7]-heterobicyclic core structure of varying composition. The five-membered ring can be pyrazole, triazole, isoxazole or isothiazole and this ring can be fused to a variety of six- or seven membered rings including but not limited to piperidinone, pyridinone, pyrimidinone, pyrimidinedione, pyranone, diazepinone, diazepinedione. The following discussion and schemes will describe methods for the syntheses of the heterobicyclic

cores and attachment of the groups "Ring D-G-G^2-G^{12}" and "Z-A-B".

The 4-aminopyrazole-5-carboxylate **V** is a useful intermediate for the preparation of many of the pyrazole fused compounds of Formulas Ia, Ib, and Ic wherein the P_4 residue is attached to a nitrogen atom of the pyrazole (Scheme I). This intermediate can be prepared in a variety of ways from aromatic hydrazines **I**. Hydrazines **I** are readily available starting materials. Specifically, they are conveniently prepared from the corresponding aniline by diazotization with $NaNO_2$ in acidic media followed by reduction of the resulting diazonium ion with a suitable reducing agent, with $SnCl_2$ being a preferred reagent. Non-aromatic hydrazines represented by **I** are readily prepared by a variety of methods, such as by displacement of a suitable halogen compound with hydrazine or with a protected hydrazine followed by deprotection.

Condensation of hydrazines **I** with a suitable hemiacetal or aldehyde followed by halogenation with NBS or NCS leads to hydrazidoyl halides **II**. Alternatively, the hydrazines **I** can be acylated with an acid chloride and converted to hydrazidoyl halides **II** by carbon tetrahalide/triphenylphosphine. The hydrazidoyl halides **II** are versatile intermediates for pyrazole synthesis (Shawali, A. S.; et. al. *J. Het. Chem.* **1980**, *17*, 833). The halide can be displaced with cyanide ion to afford cyanide **III**. Cyano compounds of this type can also be prepared more directly by diazotization of aniline **IV** followed by direct reaction with a cyano-containing active methylene compound, where R^{1a} can include a variety of groups such as ester, ketone, cyano, trifluoromethyl, sulfone, aryl, etc. (Butler, R. N.; et. al. *J. Chem. Soc. Chem. Commun.* **1992**, *20*, 1481).

Treatment of **III** with a bromoacetate in the presence of a suitable base such as carbonate or trialkylamine results

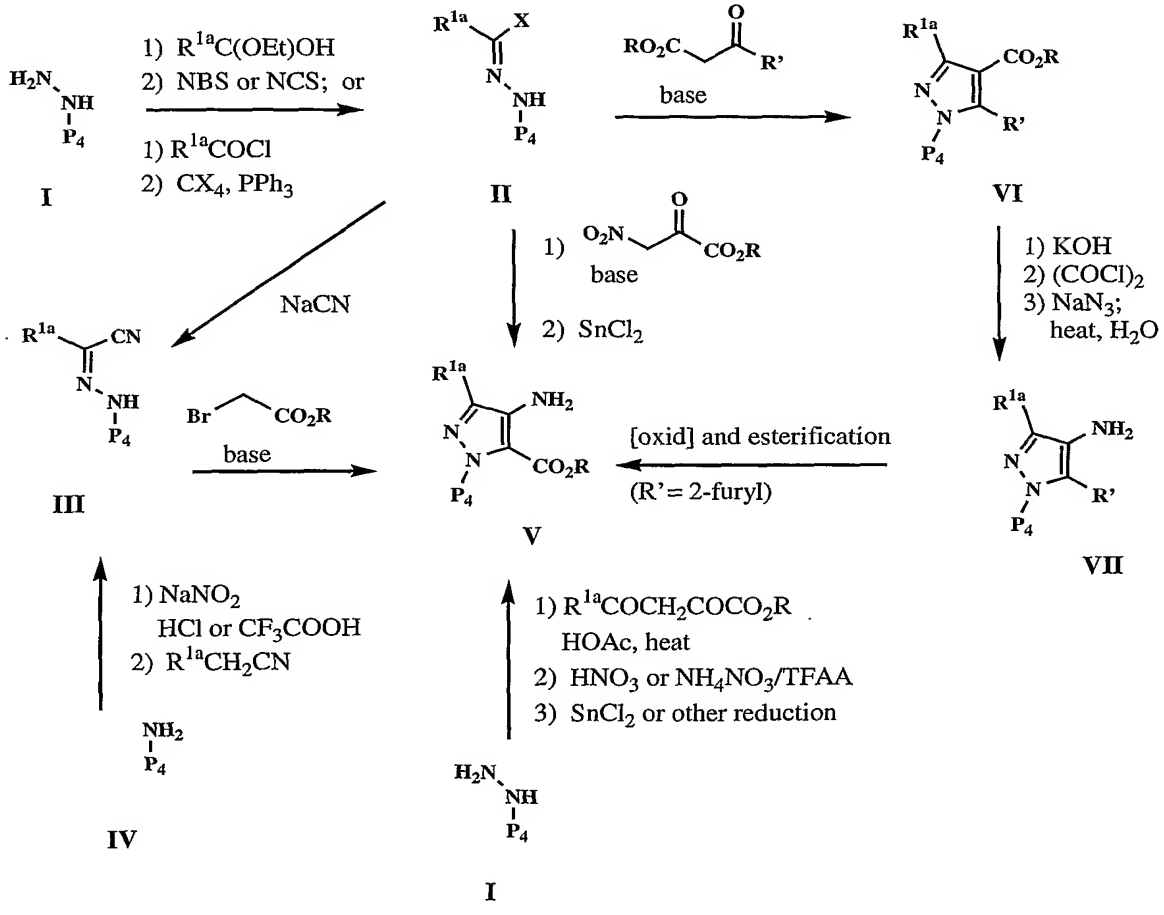
in N-alkylation followed by ring closure to give the 4-aminopyrazole-5-carboxylate **V**. Alternatively, treatment of **II** with a nitropyruvate in the presence of a base such as alkoxide provides a 4-nitropyrazole by displacement of the halide followed by ring closure of the nitrogen onto the carbonyl group. Reduction of the nitro group can be accomplished by a variety of reducing agents, a preferred one of which is $SnCl_2$, to give the 4-aminopyrazole-5-carboxylate **V**.

The hyrazidoyl halide **II** can also be reacted with a ketoester where R' represents a masked ester, preferably a 2-furyl residue, to give a pyrazole-4-carboxylate **VI**. Ester hydrolysis, conversion to an acyl azide, either via the acid chloride or anhydride, heating to generate an isocyanate via Curtius rearrangement, and finally treatment with water affords the 4-aminopyrazole **VII**. Alternatively, the amino can be masked as an appropriate carbamate by using an alcohol instead of water in the Curtius rearrangement. When R' = 2-furyl, the furan can be oxidatively cleaved under a variety of conditions, such as sodium periodate with catalytic ruthenium trichloride, or $KMnO_4$, to afford a carboxylic acid which can be esterified to afford the 4-aminopyrazole-5-carboxylate **V**.

Another route to the 4-aminopyrazole **V** involves condensation of the hydrazine **I** with an appropriate diketone or monoprotected diketone to form a 3,5-disubstituted pyrazole in which the 5-substituent is a carboxylic ester. Usually, this pyrazole can be selectively nitrated at the 4-position with nitrating agents such as nitric acid or ammonium nitrate/trifluoroacetic anhydride. Reduction of the nitro group under a variety of conditions, such as with tin (II) chloride or catalytic hydrogenation, affords the 4-aminopyrazole **V**. This route can also be carried out using a diketone with a 2-furyl group as a latent carboxylate,

giving initially a 3,5-disubstituted pyrazole in which the 5-substituent is the 2-furyl group. Oxidative cleavage of the furyl group to a carboxylate, nitration of the pyrazole 4-position, esterification and nitro reduction then affords 4-aminopyrazole **V**. It will be recognized by those skilled in the art that the synthetic route chosen to **V** will depend on additional functionality present in the molecule of interest and the route may require additional protection/ deprotection sequences as well as modifications in the order of synthetic steps.

Scheme I



In Scheme II is shown how the 4-aminopyrazole-5-carboxylate **V** can be utilized to prepare a variety of structures described by Formulas Ia, Ib, and Ic where the A-

B residue is connected to a nitrogen atom of the bicyclic core. The 4-amino group can be protected as a suitable carbamate (see Greene and Wuts, *Protective Groups in Organic Synthesis*, Wiley and Sons, **1991**) or as an azide group ($NaNO_2$, acid, NaN_3). In some cases it may not be necessary to protect the amino functionality, as will be recognized by those skilled in the art. Unmasking of the ester residue involves either basic hydrolysis (R = Me, Et), hydrogenolysis (R = Bn) or trifluoroacetic acid (R = *t*-Bu). Coupling of the resulting acid with the appropriate amine H_2N-A-B can be accomplished by a wide variety of methods known to those skilled in the art, including dicyclohexylcarbodiimide and N,N-dimethylaminopyridine, the mixed anhydride method, and the BOP reagent. Alternatively, the amide bond can be formed directly from the ester (R = Me, Et) by reacting the ester with an aluminum reagent prepared from the amine H_2N-A-B and trimethylaluminum. Deprotection of the amino group, if required, provides compounds **VIII**. Treating this amino amide with carbonyl diimidazole or other phosgene equivalent, such as triphosgene, provides pyrazolopyrimidinediones **IX**. Alternatively, aminocarboxylate **V** can be converted to pyrazolopyrimidinediones **IX** in a single step by heating with an appropriate isocyanate OCN-A-B in the presence of a base such as sodium hydride.

Treating **VIII** with a substituted bromoacetyl chloride or bromide in the presence of a base such as triethylamine affords the pyrazolodiazepinediones **X**. Refluxing **VIII** in the presence of formic acid provides the pyrazolopyrimidinones **XI** (R^3 = H). Substituted derivatives **XI** can be obtained by refluxing **VIII** in the presence of triethylorthoacetate (R^3 = Me) or other orthoesters. Reduction of **XI** with catalytic hydrogenation, sodium

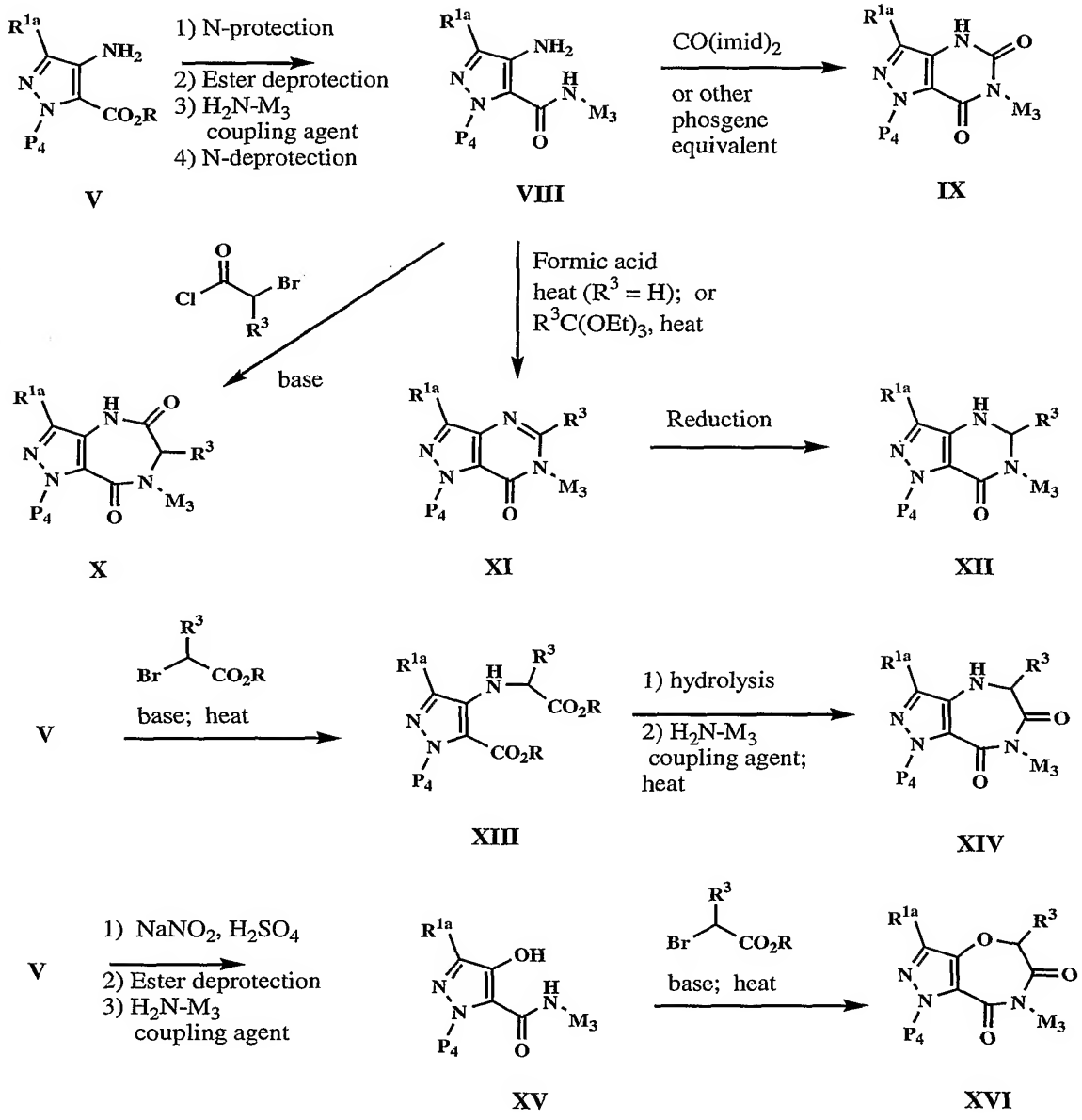
borohydride in acidic medium or other reducing agent can provide compounds of type **XII**.

Additionally, **V** can be treated with a bromoacetate in the presence of a base such as carbonate or sodium hydride to provide **XIII**. Selective hydrolysis of either ester of **XIII** followed by standard coupling with H_2N-A-B and subsequent heating affords compounds **XIV**, which are regioisomeric with **X**.

Oxygen analogs of **XIV** are prepared by converting the amino group of **V** to a hydroxy group via a diazonium ion. Coupling with the amine H_2N-A-B by any of a wide variety of procedures yields **XV**. O-alkylation of **XV** with a bromoacetate in the presence of a base such as sodium hydride leads to **XVI**, the oxygen analogs of **XIV**.

In the cases of compounds **IX**, **X**, **XII** and **XIV** the nitrogen atom can be further functionalized to provide additional analogs, such as by treating with methyl iodide in the presence of a base to afford the N-methyl derivatives.

Scheme II



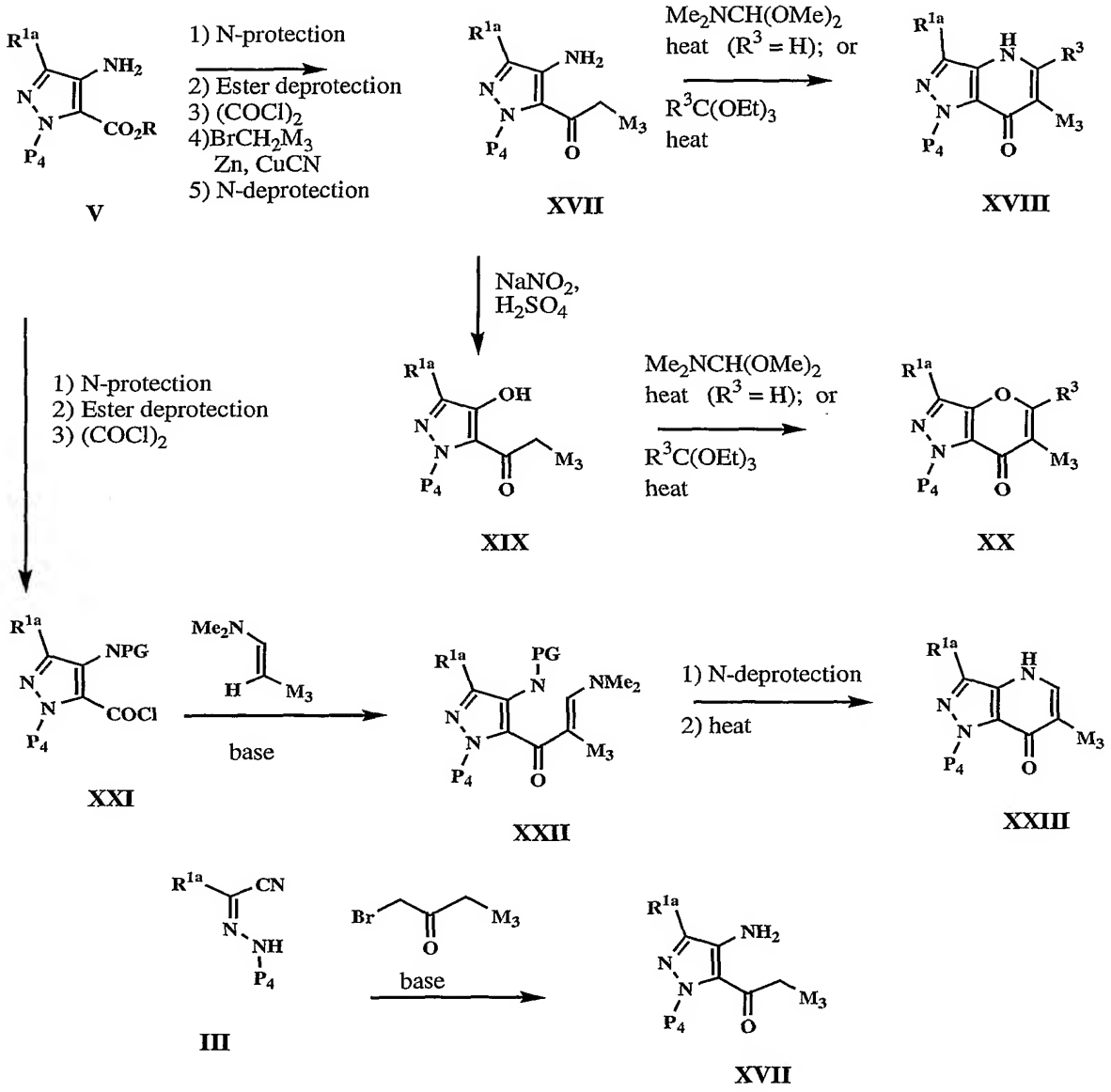
The 4-aminopyrazole-5-carboxylate can be used to prepare pyrazolopyranone and pyrazolopyridinone derivatives, in which the A-B residue is attached to a carbon atom of the bicyclic core, as shown in Scheme III. N-protection of **V** as described previously can be followed by straightforward conversion of the ester residue to an acid chloride. Treatment of this acid chloride with a zinc cuprate reagent

derived from Br-CH_2-M_3 (the connecting portion of M_3 being aryl) will afford the ketone **XVII** after N-deprotection. Heating **XVII** with dimethylformamide dimethylacetal or with an orthoester can provide the pyrazolopyridinone compounds **XVIII**. Conversion of the 4-amino residue of **XVII** to a hydroxyl group via the diazonium ion will lead to **XIX**, which will provide the pyrazolopyranone derivatives **XX** under similar cyclization conditions.

Alternatively, treatment of the acid chloride **XXI**, obtained as described above where N-PG can represent a carbamate protected nitrogen or can represent conversion of the amino group to an azide group as described previously, with a suitable enamine in the presence of a base such as triethylamine can afford the ketone **XXII**. N-deprotection followed by heating will afford the pyrazolopyridinones **XXIII** (**XVIII** where R^3 = H).

Also, the ketone **XVII** can be prepared from the cyano compound **III** by treatment with a suitable bromoketone in the presence of a base such as carbonate or triethylamine. The required bromoketone is readily available by treating an appropriate acid chloride with diazomethane followed by HBr. It will be recognized by those skilled in the art that the syntheses of the compounds described in Scheme III may require additional protection/deprotection steps or modifications in the order of carrying out the steps, depending on additional functionality present in the compounds of interest.

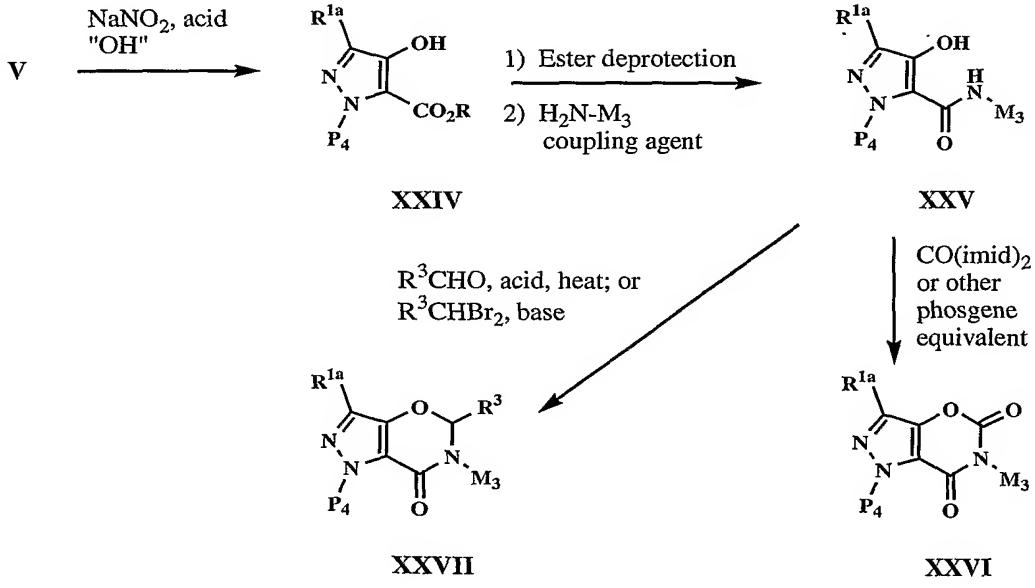
Scheme III



Additional oxygen-containing bicyclic systems can be prepared as shown in Scheme IV. The 4-amino-5-carboxylate **V** can be converted to its 4-hydroxy derivative via the diazonium ion to give **XXIV**. Ester deprotection and amide bond formation with an appropriate H_2N-M_3 as described in Scheme II will afford the amide **XXV**. Alternatively, the amide bond can be formed directly from the ester by addition of the aluminum reagent derived from H_2N-M_3 and

trimethylaluminum. The 4-hydroxy substituent can be easily protected if required by any of a number of protecting groups, such as with *t*-butyldimethylsilyl ether (TBS), and then deprotected following amide bond formation. Treating the hydroxy amide **XXV** with carbonyl diimidazole or other phosgene equivalent, such as triphosgene, can provide the bicyclic core **XXVI**. Heating **XXV** in the presence of paraformaldehyde in the presence of a suitable acid such as *p*-toluenesulfonic acid will provide **XXVII** (R^3 = H). Alternatively, **XXV** can be treated with dibromomethane in the presence of a suitable base such as carbonate to afford **XXVII** (R^3 = H). Other aldehydes and substituted dibromomethanes can provide substituted derivatives of **XXVII** where R^3 is not hydrogen.

Scheme IV



Additional bicyclic systems in which the M_3 residue is substituted on a carbon atom can be prepared as shown in Scheme V. N-protection of 4-aminopyrazole-5-carboxylate **V**

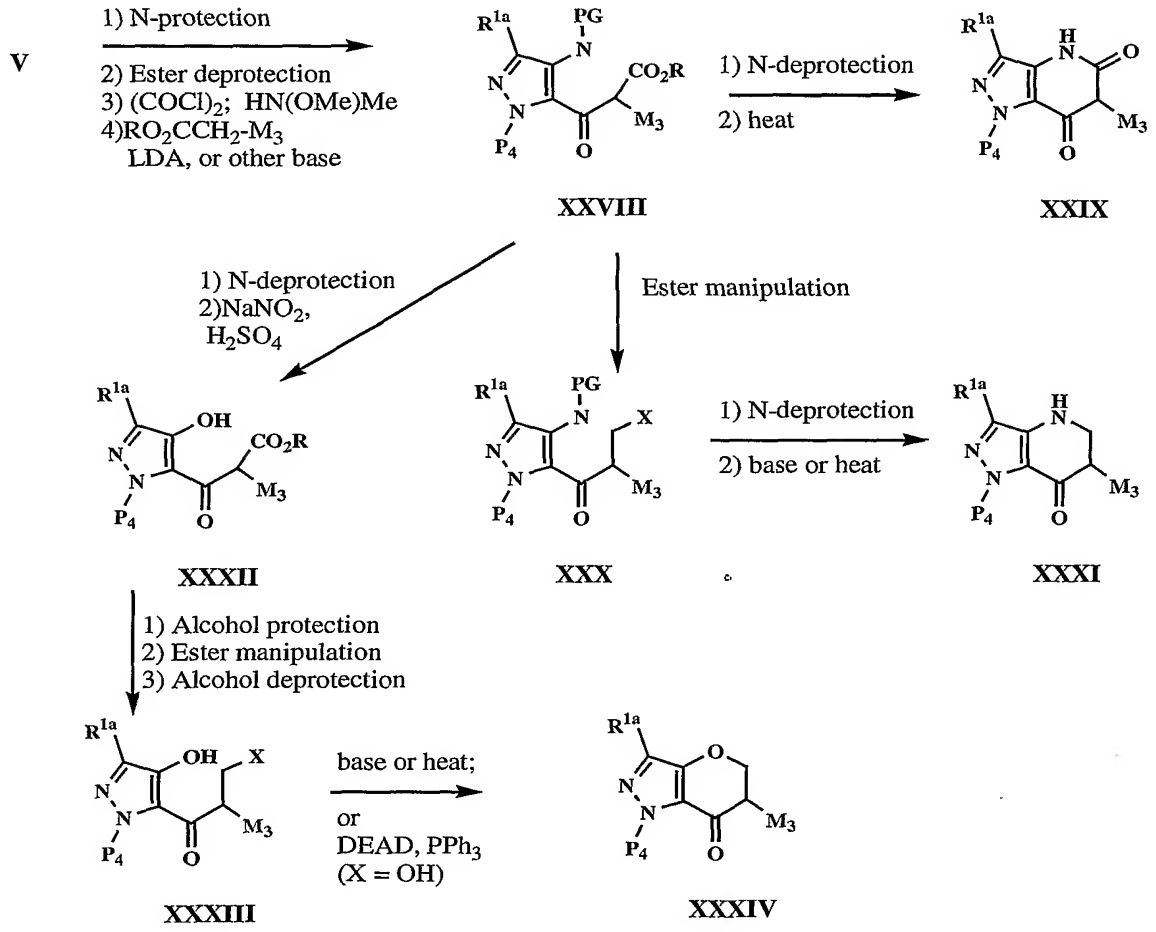
can be followed by manipulation of the ester to afford an acid chloride or an N-methoxy-N-methyl amide. Addition of an enolate derived from RO_2CCH_2-M_3 and a base such as lithium diisopropylamide or lithium hexamethyldisilazide provides **XXVIII**. The N-methoxy-N-methyl amide is the preferred reaction partner for this addition, as this functionality prevents the formation of overaddition products. Alternatively, the enolate addition reaction could be done on the ester as well. N-Deprotection of the 4-amino substituent allows it to close onto the ester residue and provides the pyrazolopiperidinedione **XXIX**.

Manipulation of the ester residue of **XXVIII** can lead to **XXX** where X represents a suitable leaving group such as a bromide or mesylate residue. A variety of methods can be utilized for the transformation of **XXVIII** to **XXX**, such as ketone protection, reduction of the ester to a primary alcohol, ketone deprotection and conversion of the primary alcohol to a bromide using CBr_4/PPh_3 or to a mesylate using methanesulfonyl chloride and a base such as triethylamine. Alternatively, the ester can be hydrolyzed to the acid that can be reduced to the primary alcohol with borane and converted to a leaving group as just described. N-deprotection liberates the 4-amino group, which provides compounds of structure **XXXI** upon heating or treatment with base.

The corresponding oxygen derivative is also available from **XXVIII**. N-deprotection, diazotization with $NaNO_2$ in acidic medium and treatment with sulfuric acid produces the 4-hydroxy derivative **XXXII**. Protection of the alcohol functionality, for example as the TBS ether, followed by ester manipulation as described above and subsequent alcohol deprotection, produces **XXXIII**. Treatment of **XXXIII** with a suitable base such as carbonate leads to ring closure to afford compounds **XXXIV**. Alternatively, compounds **XXXIII**

where X = OH can be closed to **XXXIV** via a Mitsunobu reaction by treatment with diethylazodicarboxylate and triphenylphosphine.

Scheme V

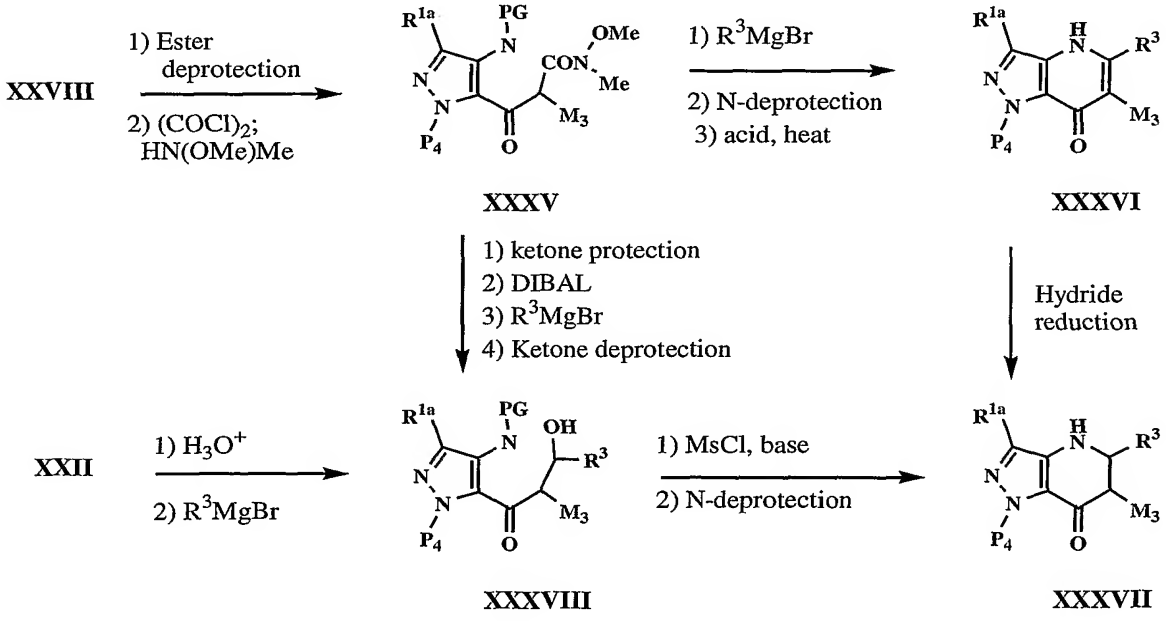


In scheme VI it is shown how to make additional bicyclic systems in which the M_3 residue is substituted on a carbon atom and the ring is substituted with an R^3 group. Ester **XXVIII** can be converted under standard conditions to the N-methoxy-N-methyl amide **XXXV**. Addition of an appropriate Grignard reagent R^3MgBr produces a ketone, which upon N-deprotection and heating in acidic conditions leads

to the substituted pyridones **XXXVI**. Hydride reduction, with REDAL for example, will produce the piperidone **XXXVII**.

Alternatively, diisobutylaluminum hydride reduction of the N-methoxy-N-methyl amide gives an aldehyde which will add a suitable Grignard reagent R^3MgBr to afford **XXXVIII**. Conversion of the alcohol to a leaving group, for example by making the mesylate with methanesulfonyl chloride and a trialkylamine base, followed by N-deprotection leads to ring closure to piperidones **XXXVII**. The alcohol **XXXVIII** can also be prepared from enamine **XXII** from Scheme III by hydrolysis to the corresponding aldehyde followed by addition of the appropriate Grignard reagent R^3MgBr.

Scheme VI

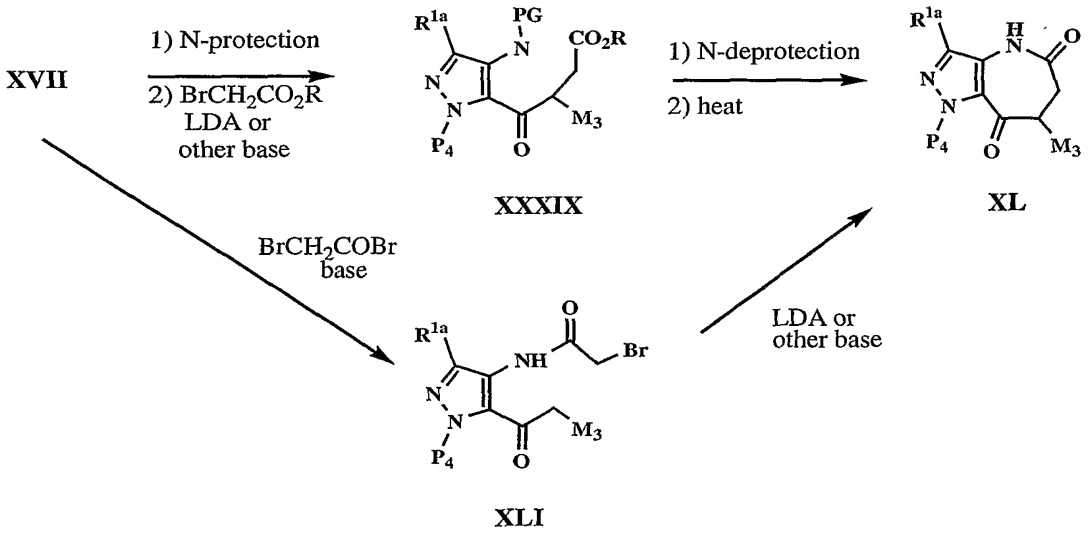


Preparation of a bicyclic system containing a seven-membered ring in which the M_3 residue is attached to a carbon atom is described in Scheme VII. N-protection of aminoketone **XVII**, where N-PG represents preferably an N-protected nitrogen wherein both N-H groups are masked, such

as by conversion to an azide group, is followed by formation of a ketone enolate, with a base such as lithium diisopropylamide, and reaction with a bromoacetate to afford **XXXIX**. N-deprotection followed by heating of the resulting amino ester affords **XL**.

Alternatively, the ester can be converted by straightforward means to a more reactive species prior to ring closure, such as a mixed anhydride or acid chloride. Treatment of **XVII** with bromoacetyl bromide and a base such as triethylamine gives the acylamine **XLI** that can be cyclized by formation of the ketone enolate with a base such as lithium diisopropylamide.

Scheme VII



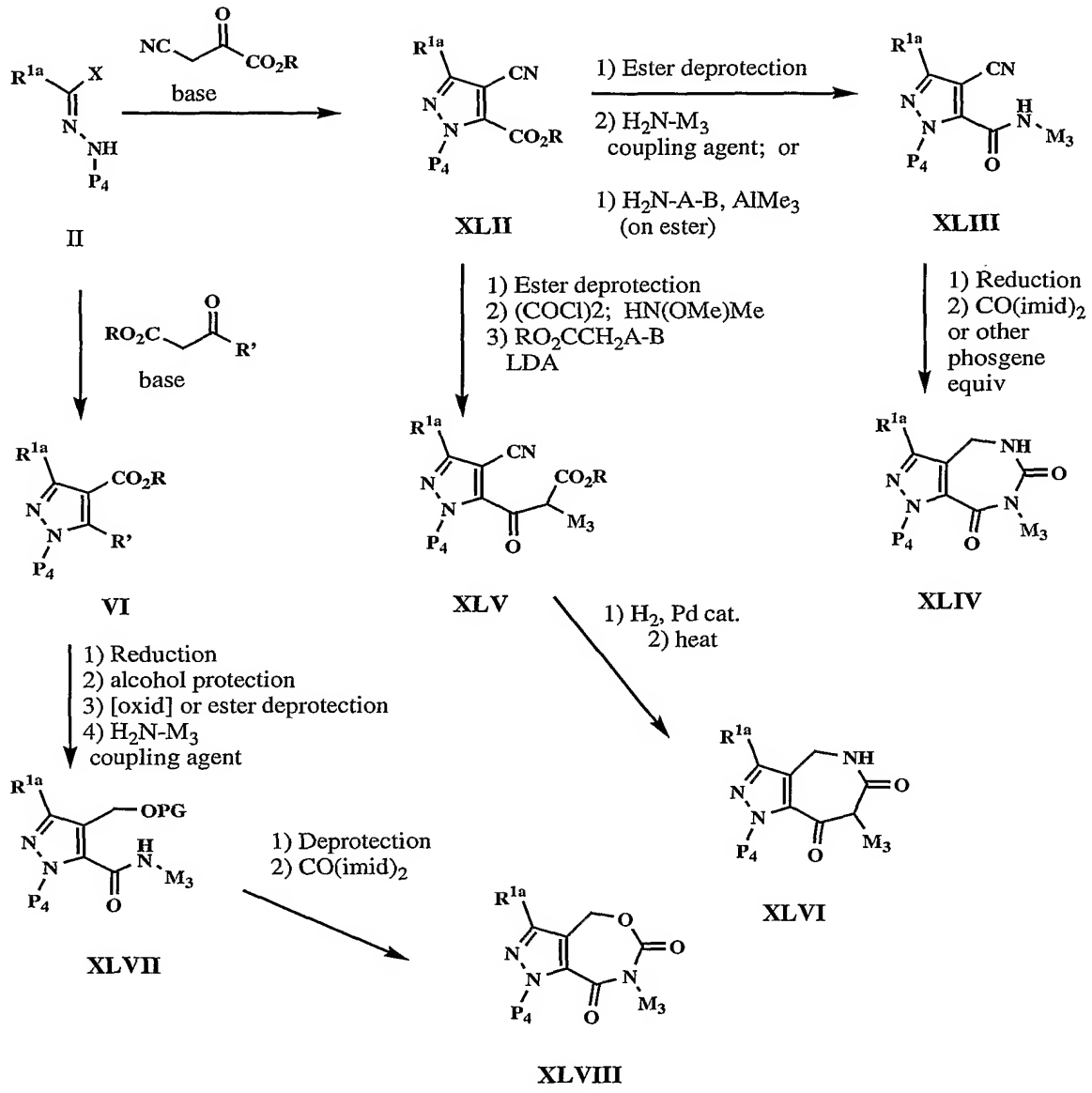
Additional seven-membered ring-containing bicyclic systems can be prepared as shown in Scheme VIII. The hydrazidoyl halide **II**, prepared as shown in Scheme I, can be cyclized with a cyanopyruvate in the presence of a base such as alkoxide to afford 4-cyanopyrazole **XLII**. Ester deprotection and coupling with H_2N-M_3 as described in previous schemes yields cyanoamide **XLIII**. Reduction of the nitrile can be accomplished by various methods, such as by

catalytic hydrogenation or by reduction with sodium borohydride in the presence of cobalt chloride. Cyclization of the resulting aminoamide using carbonyl diimidazole or other phosgene equivalent as described previously affords compounds **XLIV**.

For the corresponding compound wherein the M_3 residue is attached to carbon, the ester **XLII** can be converted to the N-methoxy-N-methyl amide as described previously. Treatment of this amide with the enolate derived from RO_2CH_2-M_3 yields the ketone **XLV**. Catalytic hydrogenation of the nitrile affords an amine that upon heating undergoes cyclization to afford **XLVI**.

The oxygen containing analog corresponding to **XLIV** is obtained from ester **VI**, prepared as described in Scheme I. The group R' represents preferably a 2-furyl residue as a masked carboxylic acid. Reduction of the ester group of **VI** with a hydride reducing agent such as diisobutylaluminum hydride is followed by protection of the resulting primary alcohol, such as by a TBS ether. When R' is 2-furyl, the carboxylic acid can be unmasked by oxidation by a variety of reagents, including ozone, potassium permanganate, and sodium periodate in the presence of ruthenium trichloride. Coupling with a suitable with H_2N-M_3 as described in previous schemes yields the amide **XLVII**. Deprotection of the alcohol affords a hydroxy amide, which can be cyclized using carbonyl diimidazole as described previously to afford compounds **XLVIII**.

Scheme VIII



Bicyclic compounds of Formulas Ia, Ib, and Ic containing a carbon atom at the pyrazole 4-position can be prepared by a [3+2] cycloaddition strategy as shown in Scheme IX (for a review of [3+2] cycloadditions, see 1,3-Dipolar Cycloaddition Chemistry (Padwa, ed.), Wiley, New York, 1984).

Treatment of unsaturated lactone **XLIX**, which is readily available by standard procedures known to those skilled in

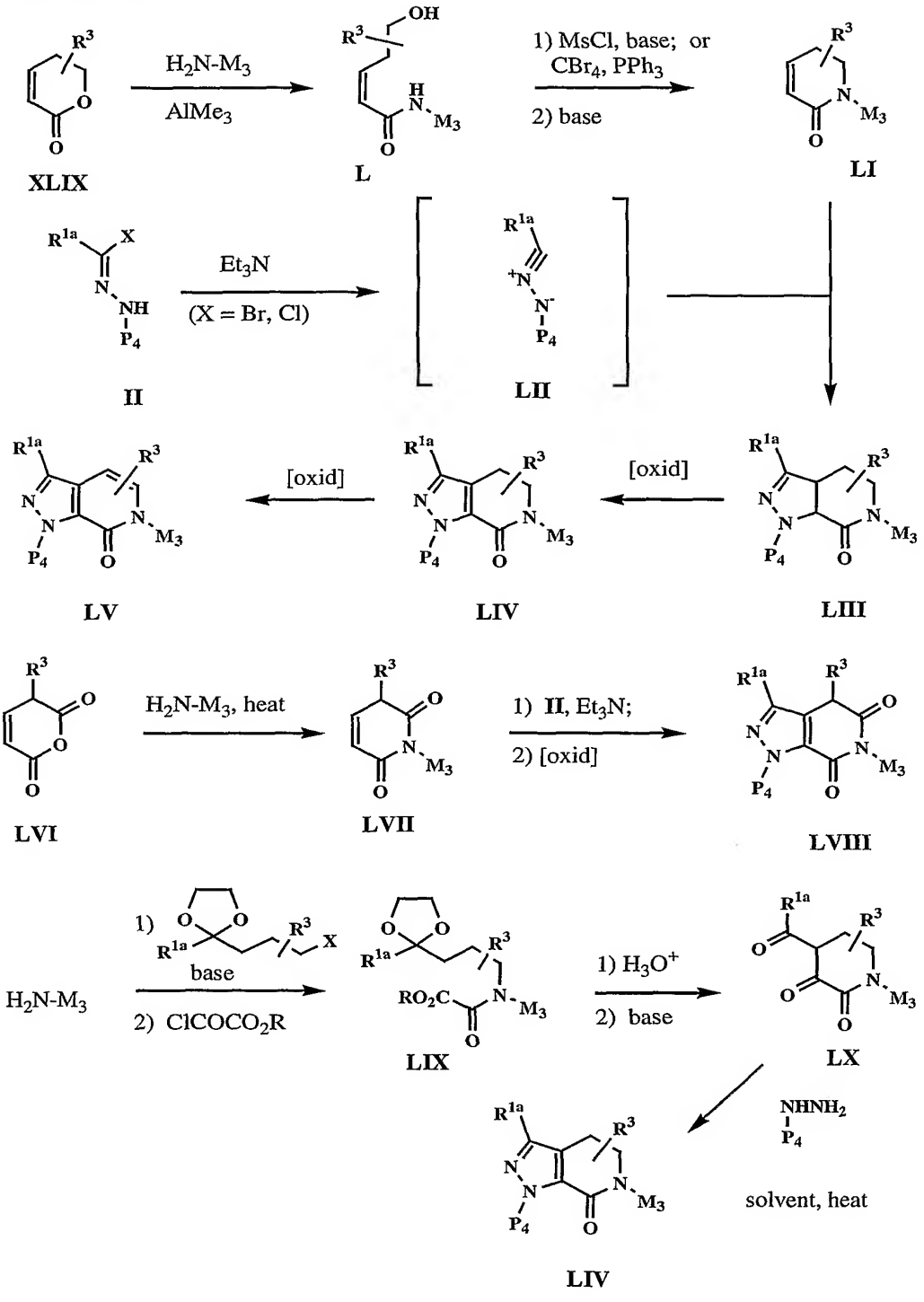
the art, with an aluminum reagent prepared from an appropriate amine H_2N-M_3 and trimethylaluminum affords the ring-opened amide **L**. Conversion of the primary alcohol under standard conditions to a suitable leaving group, such as a bromide or mesylate, and subjection to basic conditions affords the required unsaturated lactam **LI**. Treatment of hydrazidoyl halide **II**, prepared as shown in Scheme I where X = Cl or Br, with triethylamine generates a 1,3-dipolar intermediate **LII**, which can undergo a [3+2] cycloaddition with the olefin **LI** to produce the bicyclic pyrazolidine **LIII** as the predominant regioisomer. Mild oxidation with reagents such as chloranil or nickel peroxide will produce the pyrazolopiperidones **LIV**. Further oxidation, such as with DDQ, can produce the unsaturated derivatives **LV**. These steps can be reversed such that initial complete oxidation to **LV** can be followed by reduction, such as by catalytic hydrogenation, to produce **LIV**. The ketone derivatives can be prepared by condensation of an appropriate amine H_2N-M_3 with the cyclic anhydride **LVI** to give **LVII**. Alternatively, a saturated derivative of **LVI** can be condensed with an appropriate amine H_2N-M_3 followed by oxidation to the unsaturated derivative **LVII**, such as by treatment with LDA/PhSeSePh and subsequent oxidative selenoxide elimination. The olefin **LVII** undergoes similar [3+2] cycloaddition to give a pyrazolidine intermediate that is readily oxidized to the pyrazolopiperidinedione derivatives **LVIII** by a variety of oxidizing agents.

An alternative preparation of compound **LIV** is also described. A standard alkylation/acylation sequence on the amine H_2N-M_3 affords amide ester **LIX**, which contains a protected ketone functionality. A variety of reaction conditions can be employed for these transformations, which are known to those skilled in the art. Deprotection of the ketone followed by Dieckmann condensation under basic

conditions affords the cyclic diketoamides **LX**. Condensation of **LX** with an appropriate hydrazine is readily accomplished by heating in a solvent such as acetic acid or ethanol to afford the previously described **LIV**.

Pyrazolopiperidone compounds **LXVI** (where n=1) wherein the pyrazole 4-substituent R^{1a} is a trifluoromethyl group can be prepared via the method outlined in Scheme X. Coupling of the acid **LXI** with amines H_2N-M_3 can be accomplished under a variety of conditions, such as via the acid chloride, giving amide **LXII**. A straightforward sequence involving cleavage of the tetrahydrofuran ring and intramolecular cyclization on the amide nitrogen affords the ketolactam **LXIII**. This compound can also be prepared from the lactam **LXIV** by introduction of sulfur substituents and subsequent oxidation to the ketolactam **LXIII**. Formation of the morpholine or related enamine followed by reaction with trifluoroacetic anhydride leads to the trifluoroacetylated intermediate **LXV**. Alternatively, dichlorination of lactam **LXIV** with PCl_5 or analogous reagents, heating with excess morpholine or related amine, and reacting the enamine derived in this way with trifluoroacetic anhydride also yields the trifluoroacetylated intermediate **LXV**. This compound can be readily condensed with an appropriate hydrazine to afford the pyrazolopiperidone compounds **LXVI**. Analogous chemistry can be utilized to afford [5,7]-fused ring systems (where n=2).

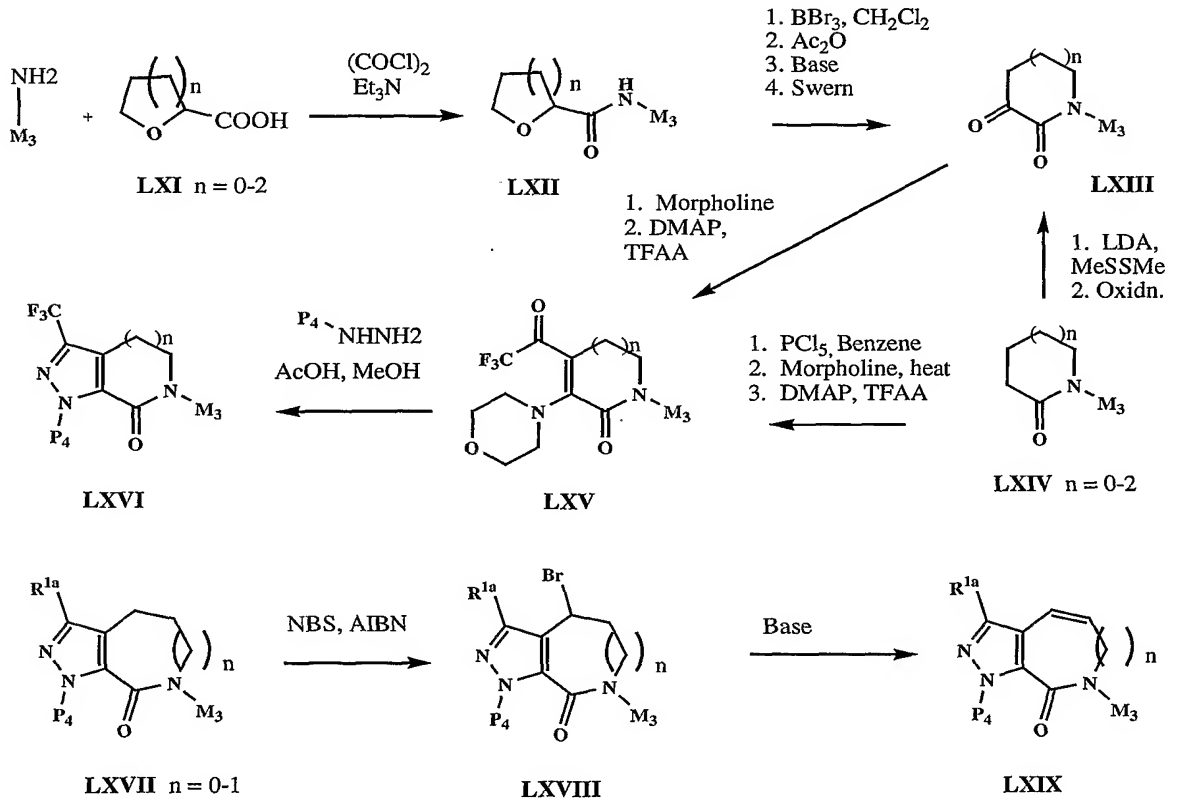
Scheme IX



Unsaturated analogs of the above compounds can be prepared as shown in the bottom of Scheme X. Bromination of **LXVII**, prepared as described in Scheme IX and the top of

Scheme X, affords bromo analog **LXVIII**. Elimination of HBr by treatment with any of a variety of bases, such as DBU, will afford the unsaturated bicylic analogs **LXIX**. Additional analogs can be prepared by displacement of the bromide **LXVIII** by any of a wide variety of nitrogen-, oxygen- and sulfur-based nucleophiles.

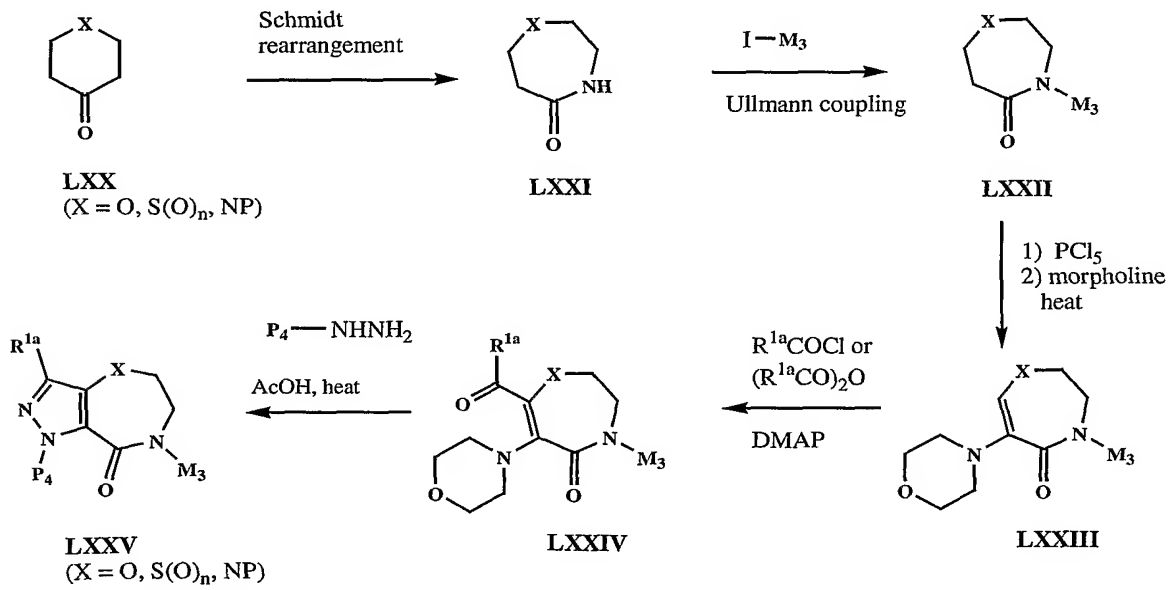
Scheme X



Additional [5,7]-fused bicyclic systems which contain an additional heteroatom in the seven-membered ring can be prepared as shown in Scheme XI. Compounds **LXXI** where X is O or S can be prepared from commercially available tetrahydro-4H-pyran-4-one and tetrahydrothiopyran-4-one. Photoinduced Schmidt rearrangement of (triisopropylsilyl)azidohydrin (Evans, P. A. and Modi, D. P. *J. Org. Chem.* **1995**, *60*, 6662-6663), which is formed from tetrahydro-4H-pyran-4-one and tetrahydrothiopyran-4-one, provides tetrahydro-1,4-oxazepin-

5(2H)-one and tetrahydro-1,4-thiazepin-5(2H)-one. Compounds **LXXI** where X is NH or NR can be prepared by Schmidt rearrangement of 4-piperidone monohydrate hydrochloride or protected 4-piperidone (Groves, J. T. and Chambers, R. R. Jr. *J. Am. Chem. Soc.* **1984**, *106*, 630-638). Ullmann coupling of the lactam with I(Br)-M_3 provides the lactam **LXXII** with an M_3 residue. Dichloronation with phosphorus pentachloride or related reagent affords a dichlorinated intermediate which can react with morpholine to give the enamine **LXXIII**. Reaction of **LXXIII** with DMAP and an appropriate acid chloride or acid anhydride provides the acylenamine intermediate **LXXIV** which can be condensed with an appropriate hydrazine in acetic acid to afford the [5,7]-fused bicyclic compounds **LXXV.**

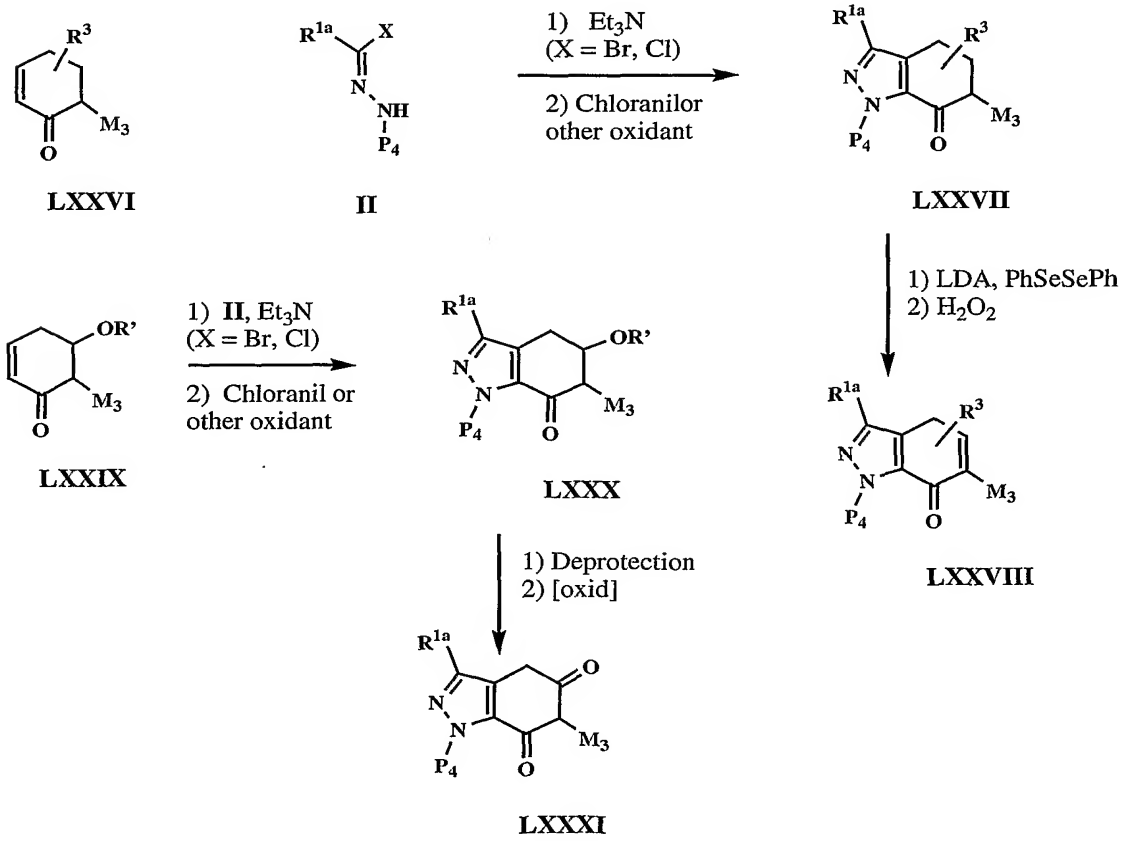
Scheme XI



Bicyclic compounds of Formulas Ia, Ib, and Ic which contain a carbon atom at the pyrazole 4-position and wherein the M_3 residue is attached to a carbon atom are also prepared by a [3+2] cycloaddition strategy as shown in Scheme XII. Unsaturated cyclic ketones **LXXVI** are readily available by standard synthetic methods known to those skilled in the art. The [3+2] cycloaddition with the 1,3-

dipole generated from **II** as described previously gives a pyrazolidine intermediate that can be readily oxidized to the pyrazolocyclohexanone **LXXVII**. Introduction of a double bond, such as by treating with LDA and PhSeSePh followed by oxidative selenoxide elimination, gives the unsaturated derivative **LXXVIII**. Incorporation of a residue such as a protected alcohol into the unsaturated ketone, represented by **LXXIX**, leads to pyrazolocyclohexanone **LXXX** following [3+2] cycloaddition and subsequent oxidation. Deprotection of the alcohol and oxidation by a variety of reagents affords the pyrazolocyclohexanedione **LXXXI**.

Scheme XII



LXXVI II LXXVII

LXXIX LXXX LXXVIII

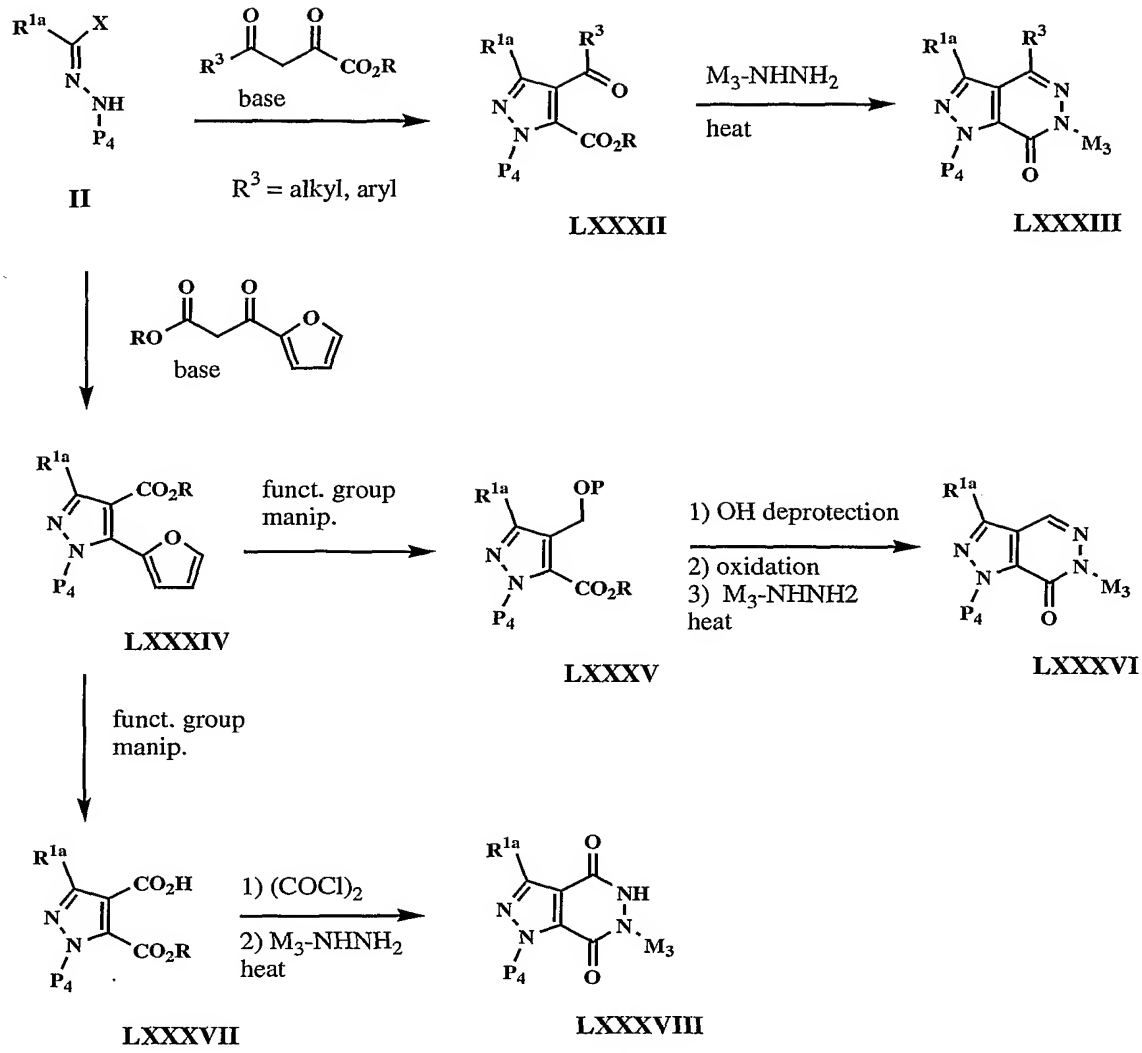
LXXXI

Additional bicyclic compounds of Formulas Ia, Ib, and Ic containing a carbon atom at the pyrazole 4-position are

described in Scheme XIII. Condensation of hydrazidoyl halide **II** with a diketoester in the presence of a base such as alkoxide affords pyrazoles **LXXXII**. Heating this ketoester in the presence of readily available hydrazines M_3-$NHNH_2$ affords the pyrazolopyridazinones **LXXXIII**.

For preparation of pyrazolopyridazinones where R^3 is hydrogen, the hydrazidoyl halide **II** can be cyclized with a furyl ketoester in the presence of alkoxide base to afford **LXXXIV**. Standard functional group manipulations, involving ester reduction and protection, furyl oxidation and esterification leads to **LXXXV**, although not necessarily in that order. Those skilled in the art will be able to determine a proper order and appropriate reagents for achieving these transformations. Alcohol deprotection and oxidation, such as by manganese dioxide, affords an aldehyde ester which readily produces **LXXXVI** upon heating in the presence of a hydrazine M_3-$NHNH_2$. Appropriate functional group manipulation of **LXXXIV**, of which many methods are available, can also afford ester acids **LXXXVII**. Activation of the carboxylic acid, such as by formation of the acid chloride with oxalyl chloride, followed by heating in the presence of a hydrazine M_3-$NHNH_2$ affords the pyrazolopyridazinedione **LXXXVIII**.

Scheme XIII



The preparation of the compounds of Formulas Ia, Ib, and Ic where the five-membered ring is triazole is accomplished using azide intermediates. Azides readily undergo [3+2] cycloaddition reactions with a variety of olefins and alkynes, and the application of this reaction to the synthesis of the triazole-fused bicyclic compounds of Formulas Ia, Ib, and Ic is shown in Scheme XIV. As described for the pyrazole-fused compounds previously, the 4-amino-1,2,3-triazole-5-carboxylate **XCII** is a particularly useful intermediate for the preparation of many of the triazole-fused bicyclic systems. The required azides **LXXXIX**

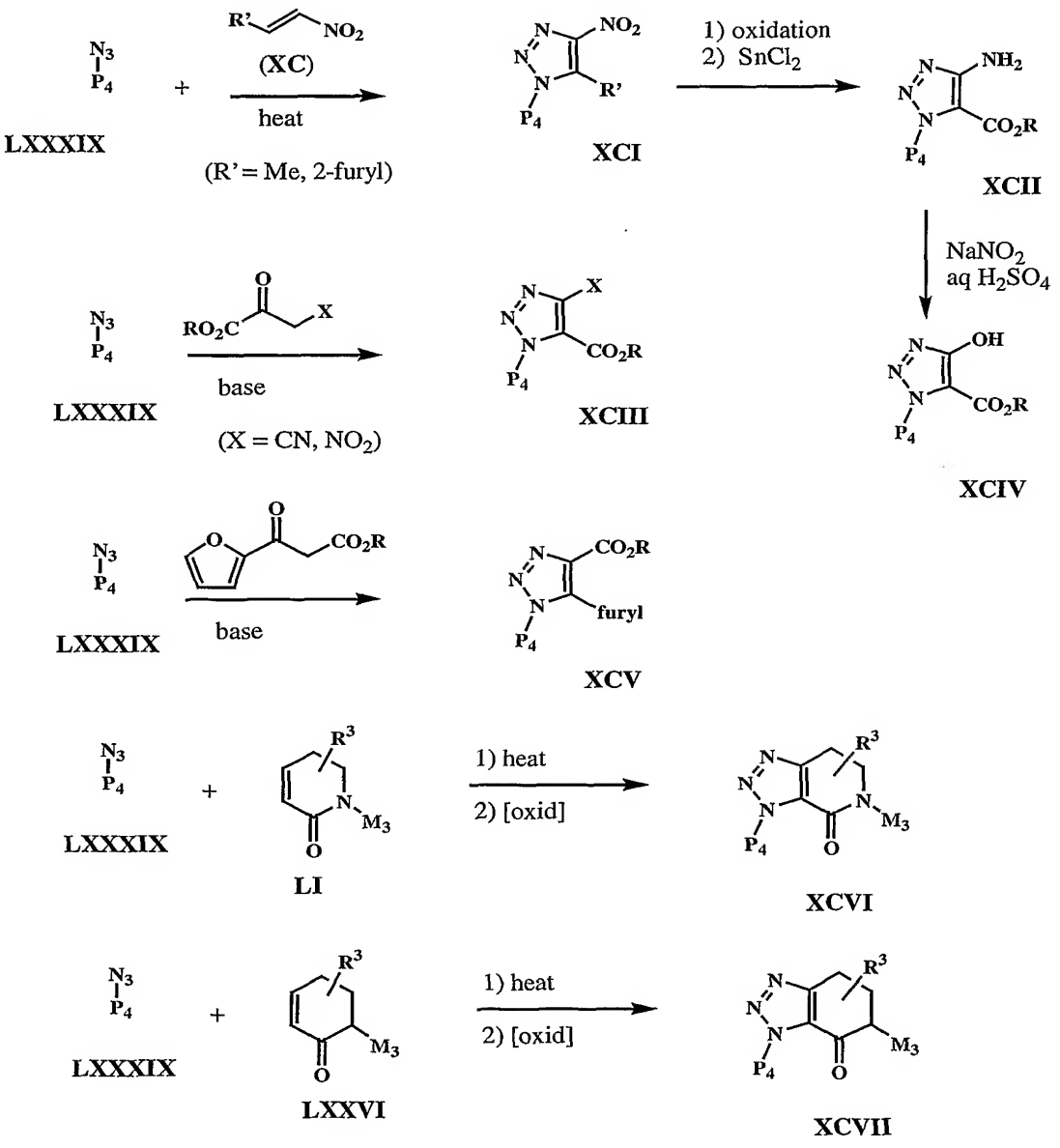
are readily available. Aliphatic azides are easily prepared from the corresponding bromide by displacement with sodium azide in solvents such as dimethylformamide and dimethyl sulfoxide. P_4 represents an aryl azide. These types of azides are readily available from the corresponding aniline by diazotization with $NaNO_2$ in acidic medium followed by displacement of the diazonium ion with sodium azide. The [3+2] cycloaddition of azides **LXXXIX** with nitroolefins **XC** (R' = Me, 2-furyl) affords the triazoles **XCI** as the major product, in which initial cyclization to a triazoline intermediate is followed by autooxidation to the triazole products (Cailleux, P.; et. al. *Bull. Soc. Chim. Belg.* **1996**, *105*, 45). These reactions can be performed in refluxing benzene or similar solvents at similar temperatures. Conversion of **XCI** to the 4-amino-1,2,3-triazole-5-carboxylate **XCII** is straightforward. When R' is methyl, oxidation of the methyl group with an oxidant such as $KMnO_4$ gives the carboxylic acid which can be esterified to an appropriate ester. Reduction of the nitro group by any of a variety of reducing agents, preferably $SnCl_2$ or catalytic hydrogenation, gives **XCII**. When R' is 2-furyl, the carboxylic acid can be unmasked by a variety of oxidizing agents, including ozone, $KMnO_4$ and sodium periodate/ruthenium trichloride, to give the carboxylic acid which can be esterified and reduced as described above to afford **XCII**. The 4-hydroxy-1,2,3-triazole-5-carboxylates can be obtained via the diazonium ion of **XCII** as described for the pyrazole series to afford **XCIV**.

The reaction of azides **LXXXIX** with active methylene compounds is also illustrated in Scheme XIV. Treating **LXXXIX** with cyano- or nitropyruvates in the presence of a base such as alkoxide affords triazoles **XCIII**. The triazole-4-carboxylate derivatives can be prepared by treating **LXXXIX** with a furyl ketoester in the presence of

alkoxide base to afford **XCV**. These reactions are analogous to those described in Scheme I for the pyrazole derivatives. The triazole-containing bicyclic systems having a carbon atom at the 4-position of the triazole can be prepared by [3+2] cycloaddition of an appropriate azide **LXXXIX** with an unsaturated lactam **LI** or an unsaturated cyclic ketone **LXXVI**. These cycloadditions are performed by heating in an appropriate solvent, such as benzene or toluene. The resulting triazoline intermediates are readily oxidized to the fused triazoles using chloroanil, nickel peroxide or other mild oxidant to give **XCVI** and **XCVII**, respectively.

The triazole intermediates **XCI**, **XCII**, **XCIII**, **XCIV**, **XCV**, **XCVI** and **XCVII** can be transformed into the final triazole-containing bicyclic compounds described by Formulas Ia, Ib, and Ic following the procedures described for the corresponding pyrazole derivatives in Schemes II-XI. The nitro group present in **XCI** and **XCIII** can correspond to the "N-PG" residue described in Schemes II-VIII, or alternatively, the nitro group can be reduced at an appropriate time and further protected as a suitable carbamate derivative or as an azido group.

Scheme XIV



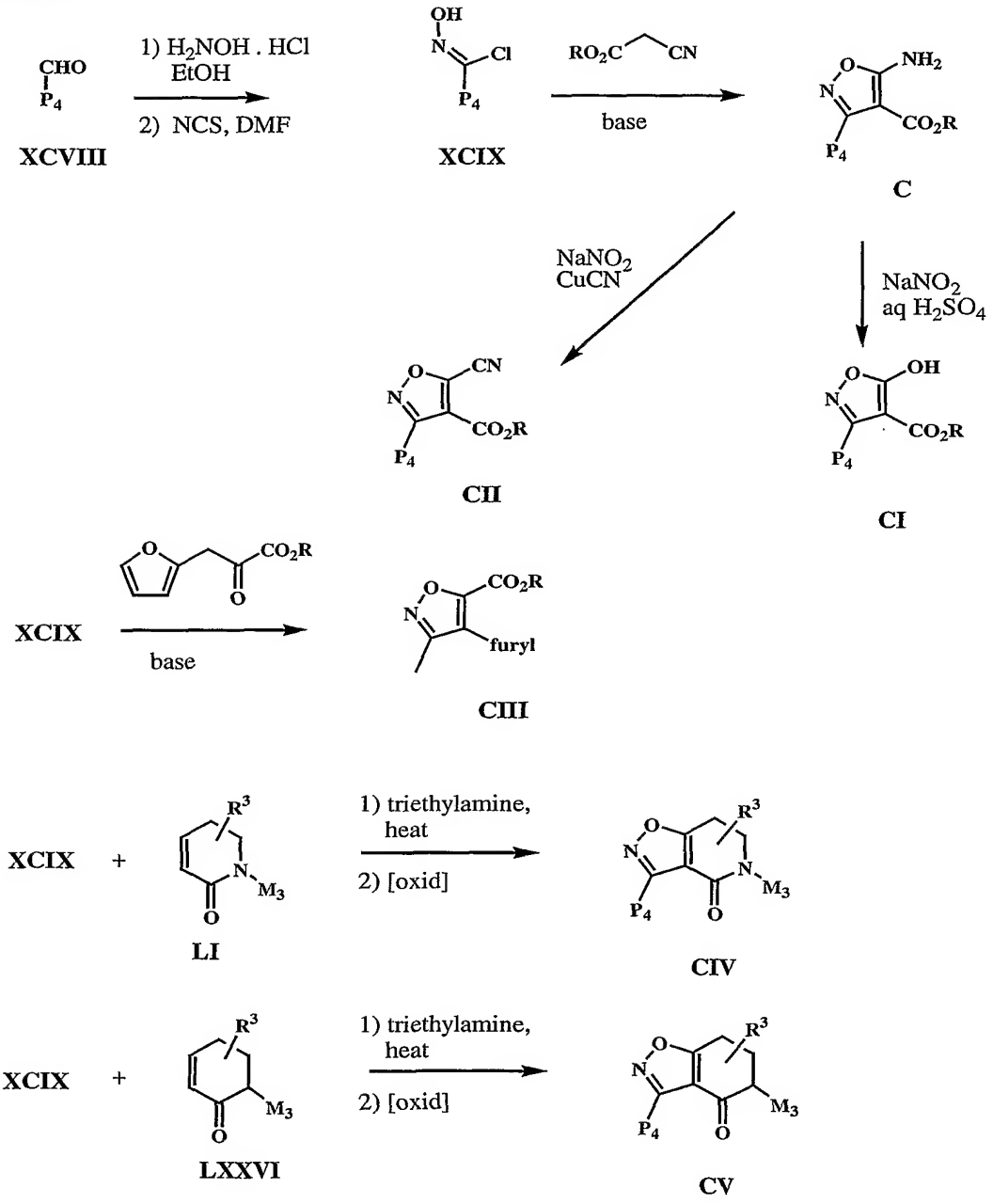
The preparation of the compounds of Formulas Ia, Ib, and Ic where the five-membered ring is isoxazole is accomplished as shown in Scheme XV. The hydroximinoyl chloride **XCIX** is a useful intermediate for the preparation of isoxazole-fused compounds. This intermediate is readily available from appropriate aldehydes **XCVIII** by oxime formation with hydroxylamine followed by chlorination with N-chlorosuccinimide. Treatment of **XCIX** with a cyanoacetate

in the presence of a base such as carbonate results in cyclization to give a 5-aminoisoxazole-4-carboxylate **C**. The amino residue of **C** can be readily converted into the corresponding hydroxy or cyano derivatives **CI** and **CII**, respectively, via the diazonium ion, as described earlier for the pyrazole and triazole compounds.

The isoxazole-5-carboxylates are available from cyclization of **XCIX** with a furan ketoester to give **CIII**. Oxidation of the furan to a carboxylic acid residue is accomplished by a variety of oxidizing agents as described earlier.

The hydroxyiminoyl chloride **XCIX** can also be treated with a base such as triethylamine to generate a nitrile oxide intermediate, which can undergo [3+2] cycloaddition reactions with appropriate olefins or alkynes. This is a convenient method by which to prepare bicyclic compounds containing a carbon atom at the 5-position of the isoxazole ring. For example, cycloaddition with the unsaturated lactam **LI** leads to formation of a fused isoxazoline intermediate which is readily oxidized with reagents such as nickel peroxide, chloranil or DDQ to afford **CIV**. Cycloaddition with unsaturated cyclic ketone and oxidation under the same conditions affords the ketone analog **CV**. The isoxazole-fused intermediates **C**, **CI**, **CII**, **CIII**, **CIV** and **CV** can be transformed into the final isoxazole-containing bicyclic compounds described by Formulas Ia, Ib, and Ic following the procedures described for the corresponding pyrazole derivatives in Schemes II-XI.

Scheme XV



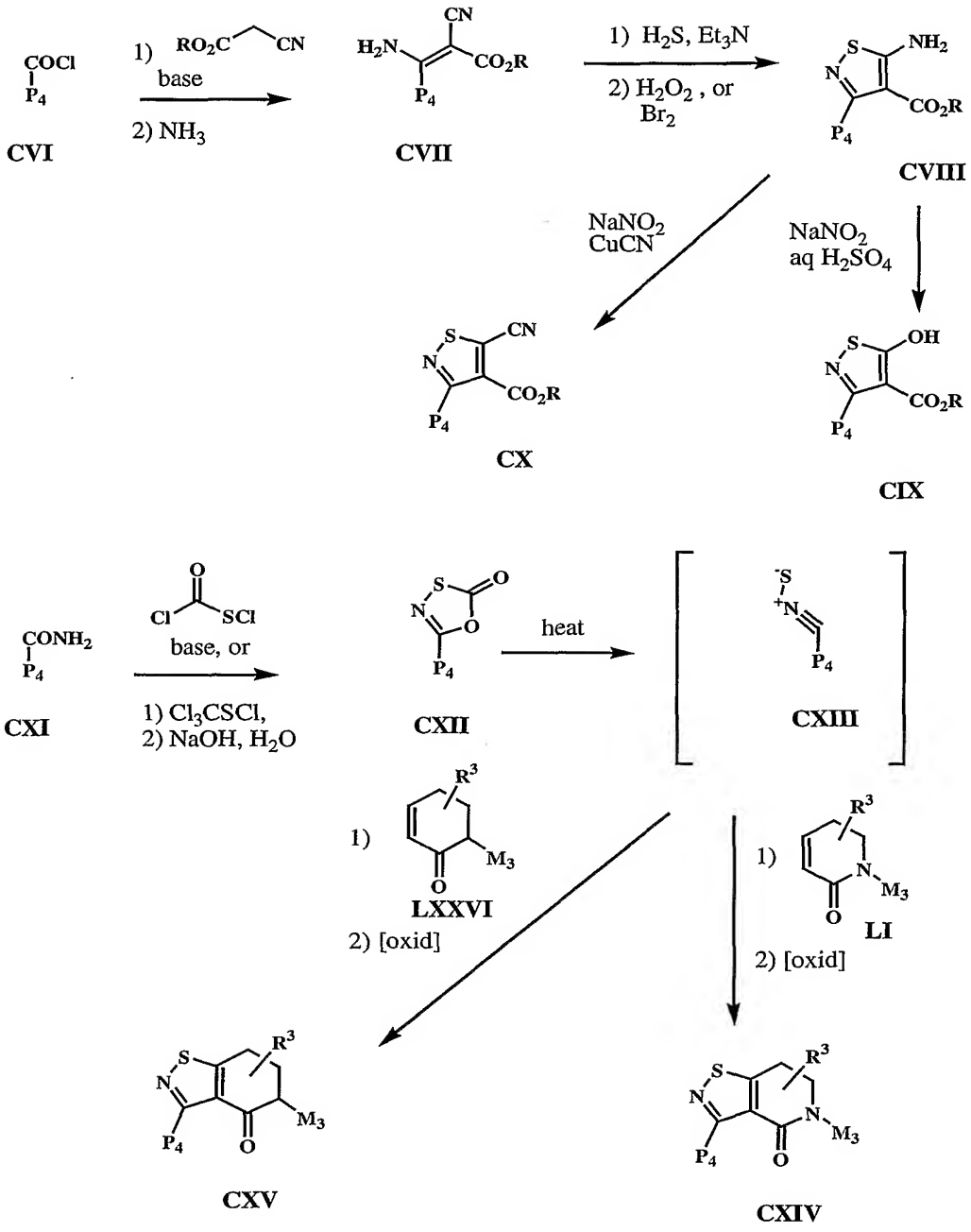
XCVIII XCIX C CII CI XCIX CIII XCIX + LI CIV XCIX + LXXVI CV

The preparation of the compounds of Formulas Ia, Ib, and Ic where the five-membered ring is isothiazole is accomplished as shown in Scheme XVI. One method for preparing the 5-aminoisothiazole-4-carboxylate intermediate **CVIII** proceeds from readily available acid chloride **CVI**. Condensation of **CVI** with a cyanoacetate in the presence of a base such as a magnesium alkoxide followed by treatment with

ammonia in an alcoholic solvent gives an aminonitrile **CVII**. Treatment with hydrogen sulfide in the presence of a base such as triethylamine affords a thioamide that can undergo an oxidative cyclization to **CVIII** upon treatment with hydrogen peroxide or bromine. As described in previous schemes, the amino residue can easily be converted into the corresponding hydroxyl or cyano derivatives **CIX** or **CX**, respectively.

Another useful intermediate for the preparation of isothiazole compounds of the present invention is the nitrile sulfide **CXIII**. This intermediate can be generated conveniently from heterocycle **CXII**, which itself can be prepared from amides **CXI** either by treating with chlorocarbonylsulfenyl chloride or by treating with trichloromethanesulfenyl chloride followed by aqueous sodium hydroxide. Thermolysis of heterocycle **CXII** affords the nitrile sulfide **CXIII**, which can undergo many of the same reactions as the corresponding nitrile oxide intermediates. For example, [3+2] cycloaddition of **CXIII** with olefins **LI** and **LXXVI** can afford, after subsequent mild oxidation as described previously, the isothiazole-fused compounds **CXIV** and **CXV**, respectively. Isothiazole intermediates **CVIII**, **CIX**, **CX**, **CXIV** and **CXV** can be transformed into the final isothiazole-containing bicyclic compounds described by Formulas Ia, Ib, and Ic following the procedures described for the corresponding pyrazole derivatives in Schemes II-XI.

Scheme XVI



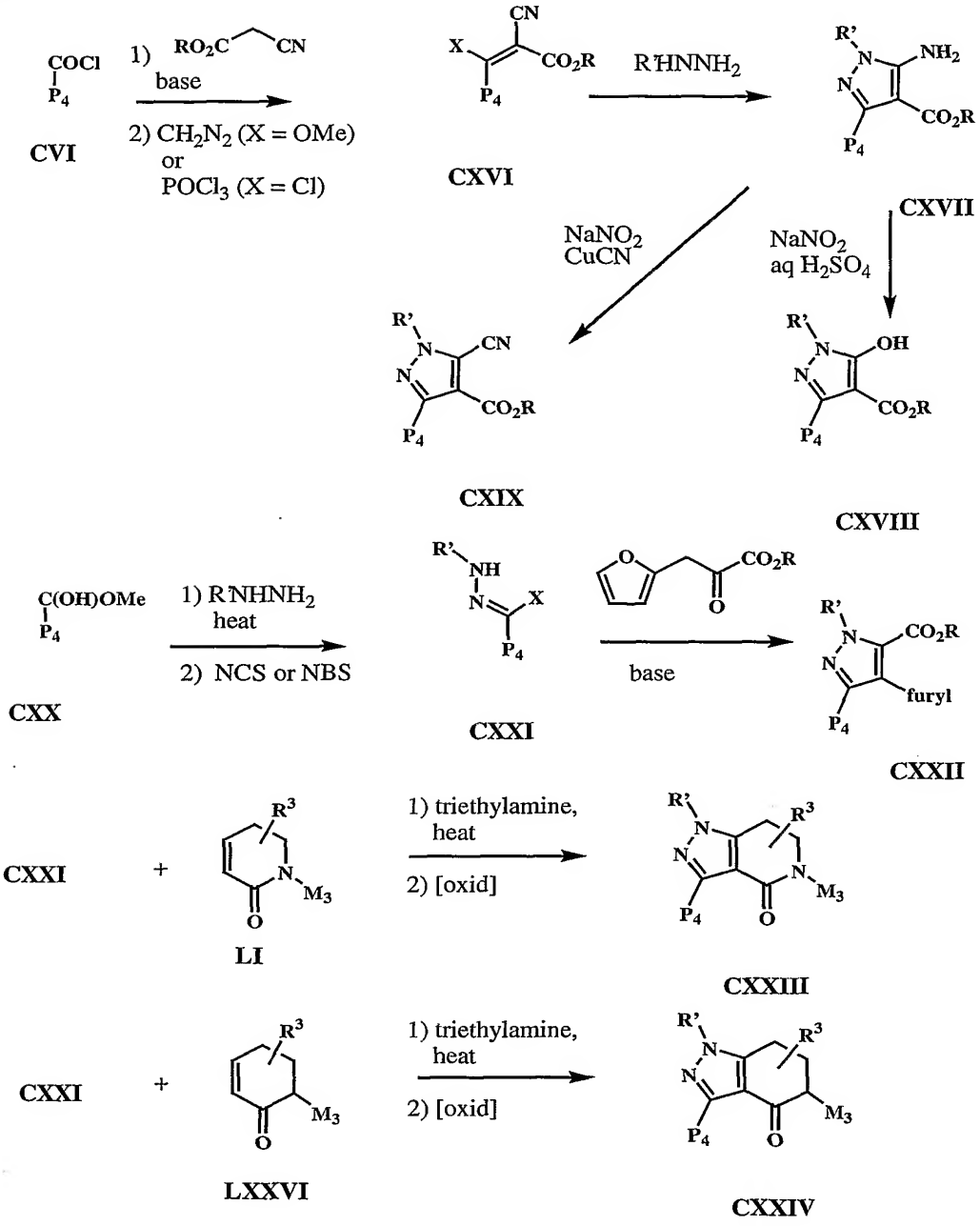
Formulas Ia, Ib, and Ic also describes pyrazole-fused bicyclic compounds in which the P_4 group resides on a carbon atom of the pyrazole ring. These compounds can be prepared as shown in Scheme XVII. Condensation of acid chlorides **CVI** with cyanoacetates in the presence of a base such as magnesium methoxide affords an enol derivative that is

converted to the enol ether **CXVI** (X = OMe) with diazomethane or to the chloro derivative **CXVI** (X = Cl) with $POCl_3$. Heating with hydrazine (R' = H) or a substituted hydrazine affords 5-amino-4-carboxylate **CXVII**. The amino residue of **CXVII** can be converted to the hydroxyl or cyano derivative **CXVIII** or **CXIX**, respectively via the diazonium ion as described previously.

The 5-carboxylate derivatives can be prepared by condensing a substituted hydrazine with a hemiacetal or related derivative represented by **CXX**. Chlorination or bromination with NCS or NBS, respectively, affords the hydrazidoyl halides **CXXI**. Reaction of **CXXI** with the anion of a furyl ketoester affords the 5-carboxylate **CXXII**, the furan residue of which can be oxidized to a carboxylic acid residue by methods described previously.

The hydrazidoyl halides **CXXI** can also participate in [3+2] cycloadditions as described previously to afford, after oxidation of the intermediate pyrazolines, the pyrazole-fused compounds **CXXIII** and **CXXIV**. The intermediates **CXVII**, **CXVIII**, **CXIX**, **CXXII**, **CXXIII** and **CXXIV** can be transformed into the final C-linked pyrazole-containing bicyclic compounds described by Formulas Ia, Ib, and Ic following the procedures described for the corresponding N-linked pyrazole derivatives in Schemes II-XI.

Scheme XVII

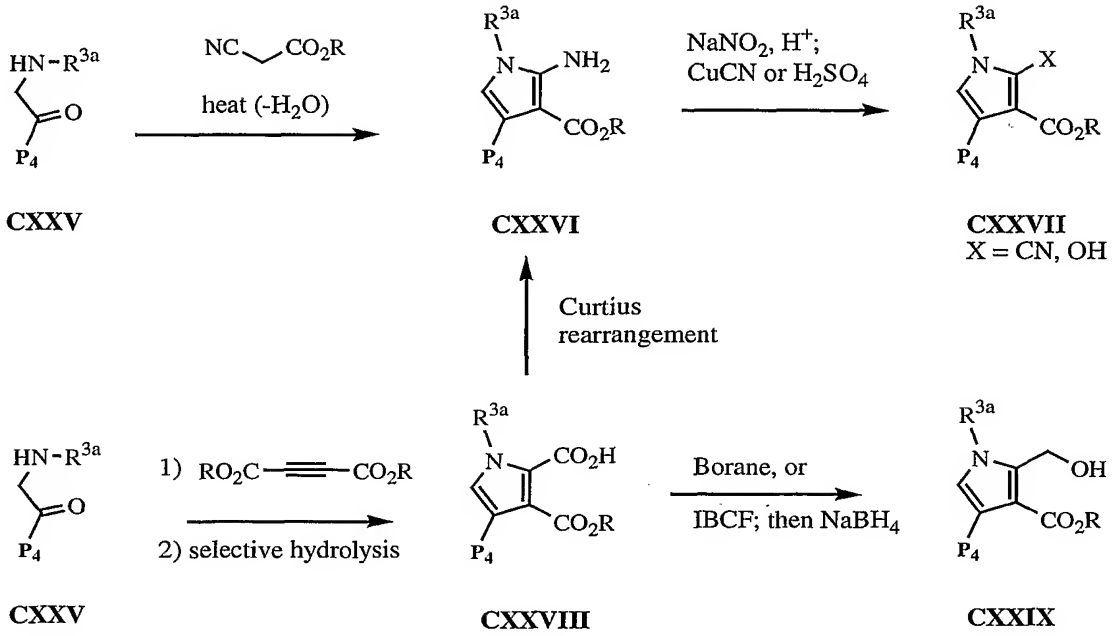


Bicyclic compounds of the present invention in which the five membered ring is pyrrole and the P_4 group is attached to a carbon atom can be prepared as shown in Scheme XVIII. For compounds of this type wherein a nitrogen atom is required at the pyrrolo 2-position, the 2-aminopyrrole **CXXVI** is a useful intermediate. This compound can be prepared by condensation of

readily obtained aminocarbonyl compounds **CXXV** with an appropriate cyanoacetate. This condensation can be carried out under basic conditions or by heating with azeotropic removal of water. The 2-aminopyrroles **CXXVI** can be diazotized and subsequently converted into the 2-cyano- and 2-hydroxypyrroles **CXXVII**, which are suitable intermediates for a variety of the bicyclic compounds of this invention.

Pyrrole 2,3-dicarboxylates can also be prepared from aminocarbonyl compounds **CXXV**. Michael addition under basic conditions with acetylenedicarboxylate esters is followed by in situ ring closure to afford the pyrrole 2,3-dicarboxylate diester. Selective hydrolysis of one of the esters, typically the 2-ester, affords the pyrrole 2-carboxylic acid **CXXVIII**. Curtius rearrangement of **CXXVIII** affords another route to the 2-aminopyrrole **CXXVI**. Also, the carboxylic acid can be reduced to the alcohol **CXXIX** using borane or by sodium borohydride reduction of the derived mixed anhydride. Following procedures described in Schemes II-VIII and Scheme XIII, the intermediates **CXXVI, CXXVII, CXXVIII** and **CXXIX** can be converted to the final pyrrolo-fused bicyclic compounds of Formulas Ia, Ib, and Ic. Other procedures not described here are also known to those skilled in the art and can be used to prepare the pyrrolo-fused bicyclic compounds of Formulas Ia, Ib, and Ic.

Scheme XVIII

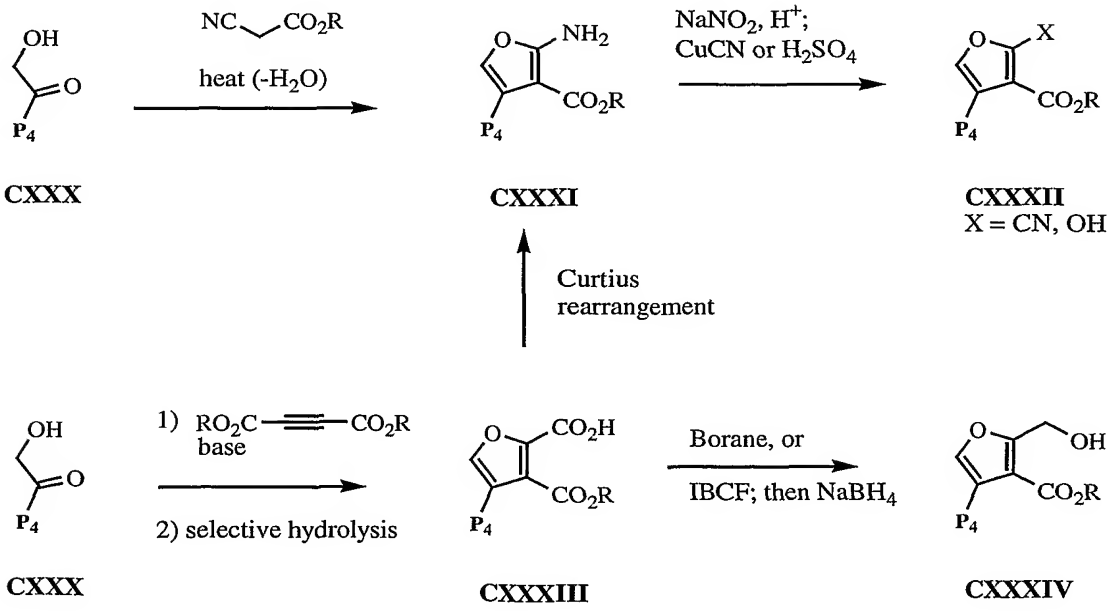


Bicyclic compounds of the present invention in which the five membered ring is furan and the P_4 is attached to a carbon atom can be prepared as shown in Scheme XIX. For compounds of this type wherein a nitrogen atom is required at the furyl 2-position, the 2-aminofuran **CXXXI** is a useful intermediate. These compounds can be prepared analogously to the pyrrole analogs described in Scheme XVIII. Thus, condensation of readily obtained hydroxycarbonyl compounds **CXXX** with an appropriate cyanoacetate affords the 2-aminofurans **CXXXI**. This condensation can be carried out under basic conditions or by heating with azeotropic removal of water. The 2-aminofurans **CXXXI** can be diazotized and subsequently converted into the 2-cyano- and 2-hydroxyfurans **CXXXII**, which are suitable intermediates for a variety of the bicyclic compounds of this invention.

Furan 2,3-dicarboxylates can also be prepared from hydroxycarbonyl compounds **CXXX**, analogously to the pyrrole analogs described in Scheme XVIII. Michael addition of **CXXX** under basic conditions with acetylenedicarboxylate esters is

followed by in situ ring closure to afford the furan 2,3-dicarboxylate diester. Selective hydrolysis of one of the esters, typically the 2-ester, affords the furan 2-carboxylic acid **CXXXIII**. Curtius rearrangement of **CXXXIII** affords another route to the 2-aminofurans **CXXXI**. Also, the carboxylic acid can be reduced to the alcohol **CXXXIV** using borane or by sodium borohydride reduction of the derived mixed anhydride. Following procedures described in Schemes II-VIII and Scheme XIII, the intermediates **CXXXI, CXXXII, CXXXIII** and **CXXXIV** can be converted to the final furan-fused bicyclic compounds of Formulas Ia, Ib, and Ic. Other procedures not described here are also known to those skilled in the art and can be used to prepare the furan-fused bicyclic compounds of Formulas Ia, Ib, and Ic.

Scheme XIX

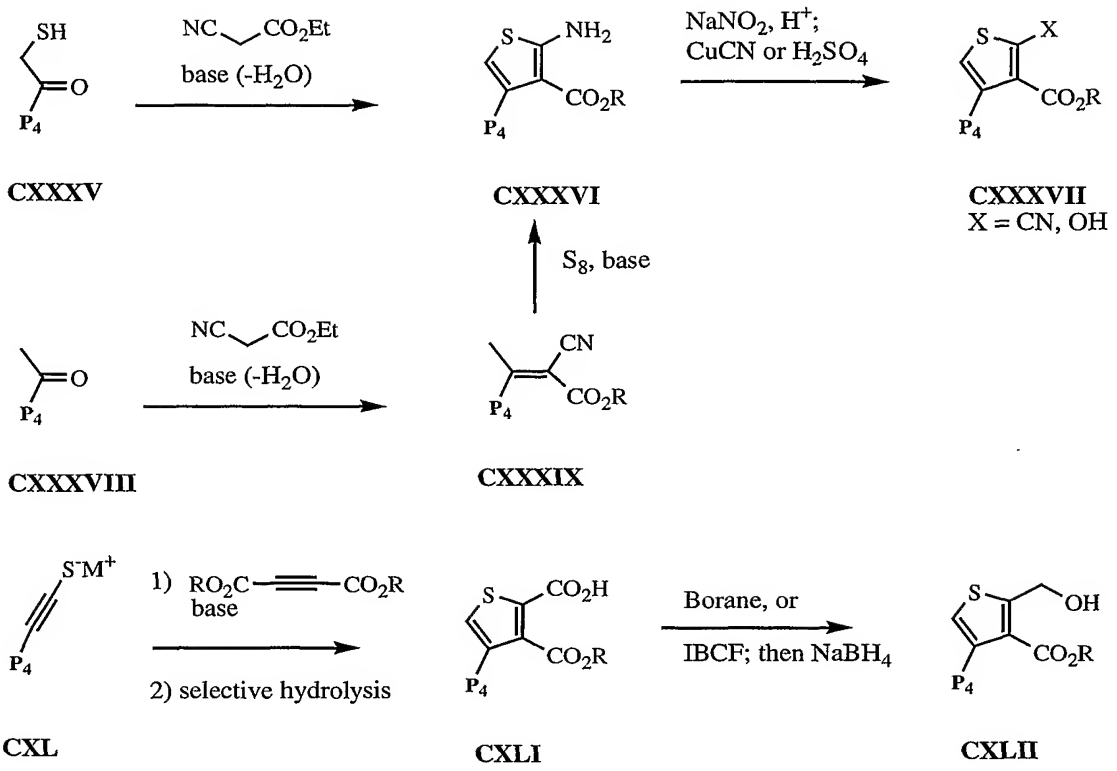


Bicyclic compounds of the present invention in which the five membered ring is thiophene and the P_4 is attached to a carbon atom can be prepared as shown in Scheme XX. For compounds of this type wherein a nitrogen atom is required at

the thiophene 2-position, the 2-aminothiophene **CXXXVI** is a useful intermediate. These compounds can be prepared analogously to the pyrrole analogs described in Scheme XVIII. Thus, condensation of readily obtained mercaptocarbonyl compounds **CXXXV** with an appropriate cyanoacetate affords the 2-aminothiophenes **CXXXVI**. This condensation can be carried out under basic conditions or by heating with azeotropic removal of water. Alternatively, condensation of the cyanoacetate with ketone **CXXXVIII** affords olefin **CXXXIX**. In a subsequent step, **CXXXIX** can be converted into 2-aminothiophenes **CXXXVI** by treatment with S_8 and a base such as triethylamine. The 2-aminothiophenes **CXXXVI** can be diazotized and subsequently converted into the 2-cyano- and 2-hydroxythiophenes **CXXXVII**, which are suitable intermediates for a variety of the bicyclic compounds of this invention.

Thiophene 2,3-dicarboxylates can be prepared from alkali-metal acetylenethiolates **CXL**. These compounds react with acetylenedicarboxylate esters in a [3+2] cycloaddition to afford thiophene 2,3-dicarboxylate diesters. Selective hydrolysis of one of the esters, typically the 2-ester, affords the thiophene 2-carboxylic acid **CXLI**. Curtius rearrangement of **CXLI** affords another route to the 2-aminothiophenes **CXXXVI**. Also, the carboxylic acid can be reduced to the alcohols **CXLII** using borane or by sodium borohydride reduction of the derived mixed anhydride. Following procedures described in Schemes II-VIII and Scheme XIII, the intermediates **CXXXVI, CXXXVII, CXLI** and **CXLII** can be converted to the final thiophene-fused bicyclic compounds of Formulas Ia, Ib, and Ic. Other procedures not described here are also known to those skilled in the art and can be used to prepare the thiophene-fused bicyclic compounds of Formulas Ia, Ib, and Ic.

Scheme XX



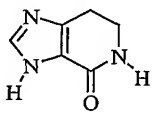
CXXXV CXXXVI CXXXVII X = CN, OH

CXXXVIII CXXXIX

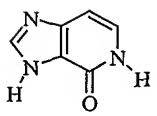
CXL CXLI CXLII

Bicyclic compounds of the present invention in which the five membered ring is imidazole and P_4 is attached to a nitrogen atom can be prepared as shown in Scheme XXI. These compounds **CXLIII** through **CLXIV**, where the R group may be alkyl, aryl or a protecting group PG, are available either from commercial sources or through known prior art and can be represented generically by **CLXV**. Suitable protection of the imidazole nitrogen affords compounds of the type **CLXVI**, which are further elaborated via a cupric mediated coupling of appropriate M_3 containing boronic acid to yield **CLXVII**. Subsequent removal of the imidazole-protecting group PG affords compounds such as **CLXVIII**. The introduction of a P_4 substituent is accomplished as before by the coupling of a P_4 containing boronic acid in a manner such that the P_4 group is transferred to the imidazole nitrogen as depicted by **CLVIX**.

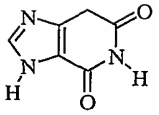
Scheme XXI



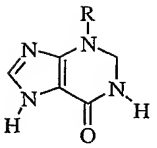
CXLIII



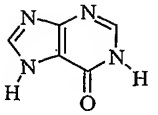
CXLIV



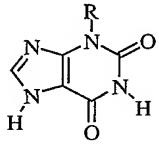
CXLV



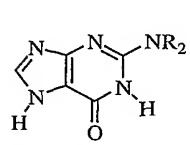
CXLVI



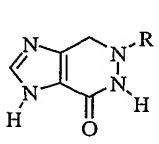
CXLVII



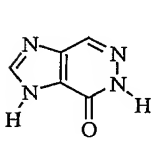
CXLVIII



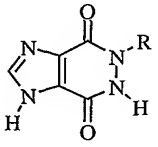
CXLIX



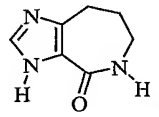
CL



CLI



CLII



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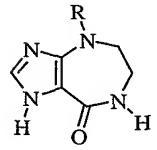
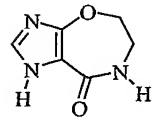
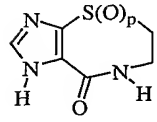


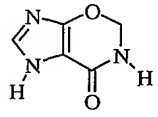
CLIV



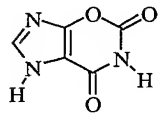
CLV



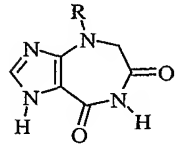
CLVI



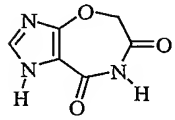
CLVII



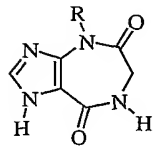
CLVIII



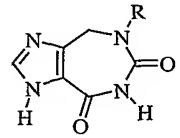
CLIX



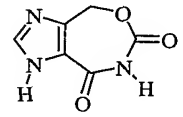
CLX



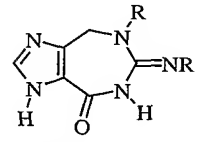
CLXI



CLXII

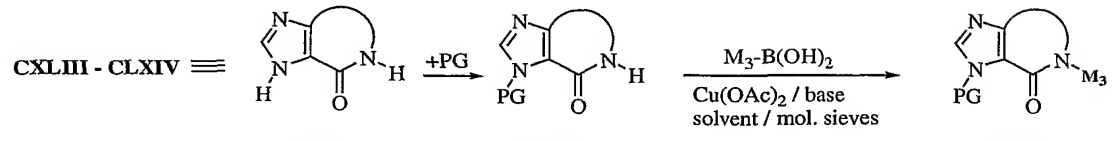


CLXIII

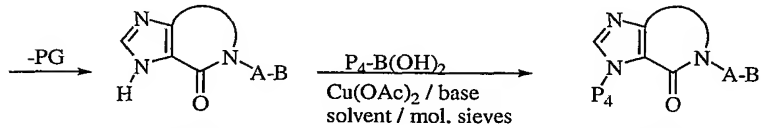


CLXIV

R = alkyl, aryl or PG



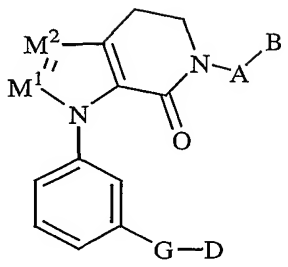
CLXV CLXVI CLXVII



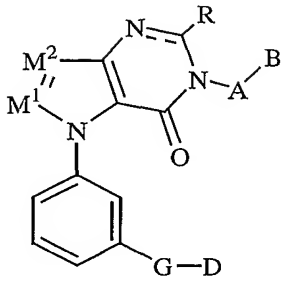
CLXVIII CLXIX

Heterocyclic systems **CXLIII** and **CXLIV**, as shown in Scheme XXII (wherein D can be -CN or halo), can be easily prepared according to the Schemes I-XXI.

Scheme XXII



CXLIII

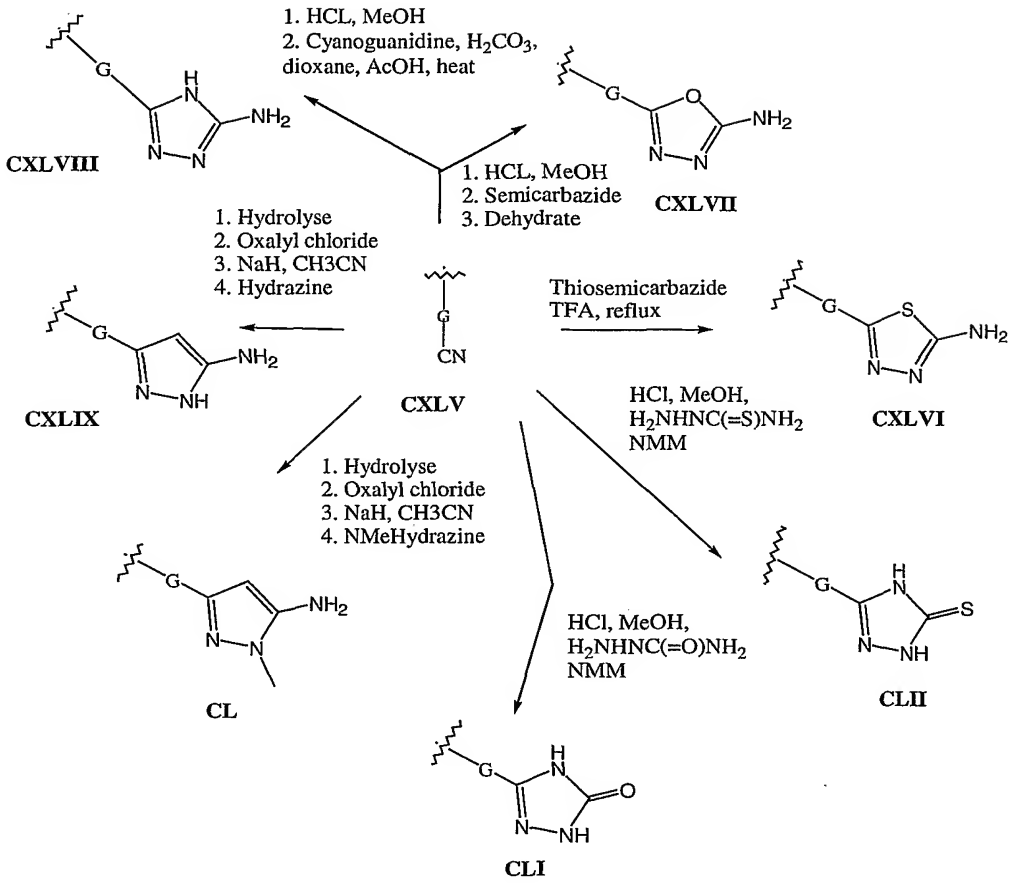


CXLIV

The compounds of the present invention have a group "A-B" and a group "G-D" attached to ring Q. Preparations of some of the "A-B" moieties can follow the same methods described in WO97/23212, WO97/30971, WO97/38984, WO98/01428, WO98/06694, WO98/28269, WO98/28282, WO98/57934, WO98/57937, and WO98/57951, the contents of which are incorporated herein by reference.

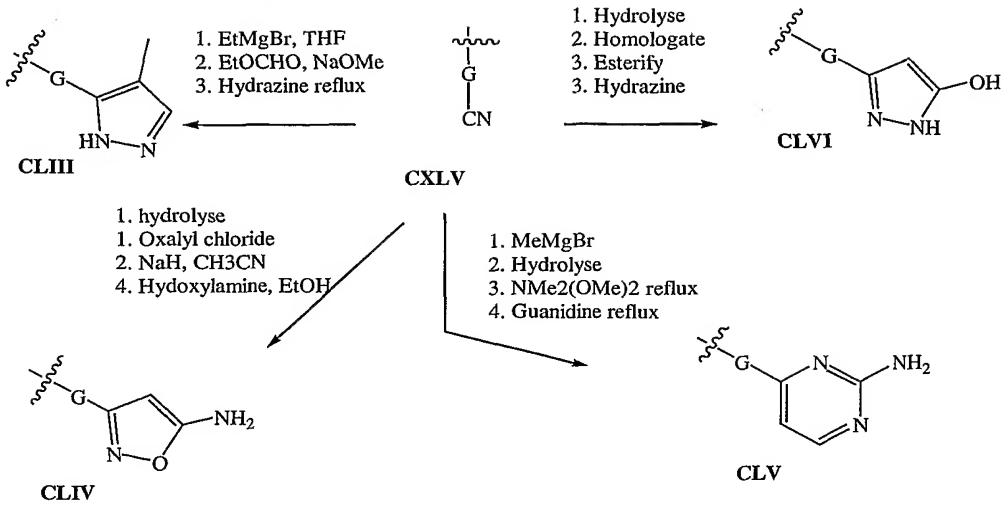
Compounds of this invention wherein G is absent and D is a cyano group **CXLV** can be easily manipulated to afford thiadiazoles **CXLVI**, oxadiazoles **CXLVII**, triazoles **CXLVIII**, pyrazoles **CXLIX-CL**, and triazolones **CLI-CLII** as outlined in Scheme XXIII.

Scheme XXIII



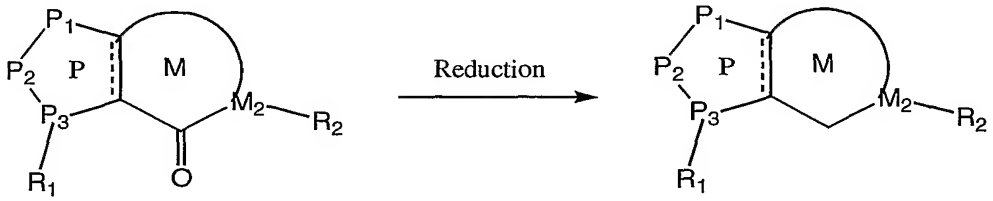
Other heterocycles contained in this invention can also be obtained via methods shown in Scheme XXIV

Scheme XXIV



The des-carbonyl compounds of this invention where M_1 is CH; can be prepared from the corresponding carbonyl intermediate A such as LIII (Scheme IX) by reduction as shown in Scheme **XX**. Further manipulation of the R1 and R2 groups would lead to the final compounds of this invention.

Scheme XXV



UTILITY

The compounds of this invention are useful as anticoagulants for the treatment or prevention of thromboembolic disorders in mammals. The term "thromboembolic disorders" as used herein includes arterial or venous cardiovascular or cerebrovascular thromboembolic disorders, including, for example, unstable angina, first or recurrent myocardial infarction, ischemic sudden death,

transient ischemic attack, stroke, atherosclerosis, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary and cerebral arterial thrombosis, cerebral embolism, kidney embolisms, and pulmonary embolisms. The anticoagulant effect of compounds of the present invention is believed to be due to inhibition of factor Xa or thrombin.

The effectiveness of compounds of the present invention as inhibitors of factor Xa was determined using purified human factor Xa and synthetic substrate. The rate of factor Xa hydrolysis of chromogenic substrate S2222 (Kabi Pharmacia, Franklin, OH) was measured both in the absence and presence of compounds of the present invention. Hydrolysis of the substrate resulted in the release of pNA, which was monitored spectrophotometrically by measuring the increase in absorbance at 405 nM. A decrease in the rate of absorbance change at 405 nm in the presence of inhibitor is indicative of enzyme inhibition. The results of this assay are expressed as inhibitory constant, K_i.

Factor Xa determinations were made in 0.10 M sodium phosphate buffer, pH 7.5, containing 0.20 M NaCl, and 0.5% PEG 8000. The Michaelis constant, K_m, for substrate hydrolysis was determined at 25°C using the method of Lineweaver and Burk. Values of K_i were determined by allowing 0.2-0.5 nM human factor Xa (Enzyme Research Laboratories, South Bend, IN) to react with the substrate (0.20 mM-1 mM) in the presence of inhibitor. Reactions were allowed to go for 30 minutes and the velocities (rate of absorbance change vs time) were measured in the time frame of 25-30 minutes. The following relationship was used to calculate K_i values:

$$(v_o - v_s)/v_s = I/(K_i\ (1+\ S/K_m))$$

where:

v_o is the velocity of the control in the absence of inhibitor;

v_s is the velocity in the presence of inhibitor;

I is the concentration of inhibitor;

K_i is the dissociation constant of the enzyme:inhibitor complex;

S is the concentration of substrate;

K_m is the Michaelis constant.

Using the methodology described above, some compounds of the present invention were found to exhibit a K_i of $\leq$10 μM, thereby confirming the utility of the compounds of the present invention as effective Xa inhibitors.

Compounds tested in the above assay are considered to be active if they exhibit a K_i of $\leq$10 μM. Preferred compounds of the present invention have K_i's of $\leq$1 μM. More preferred compounds of the present invention have K_i's of $\leq$0.1 μM. Even more preferred compounds of the present invention have K_i's of $\leq$0.01 μM. Still more preferred compounds of the present invention have K_i's of $\leq$0.001 μM.

The antithrombotic effect of compounds of the present invention can be demonstrated in a rabbit arterio-venous (AV) shunt thrombosis model. In this model, rabbits weighing 2-3 kg anesthetized with a mixture of xylazine (10 mg/kg i.m.) and ketamine (50 mg/kg i.m.) are used. A saline-filled AV shunt device is connected between the femoral arterial and the femoral venous cannulae. The AV shunt device consists of a piece of 6-cm tygon tubing that contains a piece of silk thread. Blood will flow from the femoral artery via the AV-shunt into the femoral vein. The exposure of flowing blood to a silk thread will induce the formation of a significant thrombus. After forty minutes, the shunt is disconnected and the silk thread covered with thrombus is weighed. Test agents or vehicle will be given (i.v., i.p., s.c., or orally) prior to the opening of the AV shunt. The percentage inhibition of thrombus formation is determined for each treatment group. The ID50 values (dose

which produces 50% inhibition of thrombus formation) are estimated by linear regression.

The compounds of the present invention may also be useful as inhibitors of serine proteases, notably human thrombin, plasma kallikrein and plasmin. Because of their inhibitory action, these compounds are indicated for use in the prevention or treatment of physiological reactions, blood coagulation and inflammation, catalyzed by the aforesaid class of enzymes. Specifically, the compounds have utility as drugs for the treatment of diseases arising from elevated thrombin activity such as myocardial infarction, and as reagents used as anticoagulants in the processing of blood to plasma for diagnostic and other commercial purposes.

Some compounds of the present invention were shown to be direct acting inhibitors of the serine protease thrombin by their ability to inhibit the cleavage of small molecule substrates by thrombin in a purified system. *In vitro* inhibition constants were determined by the method described by Kettner et al. in *J. Biol. Chem.* **1990**, *265*, 18289-18297, herein incorporated by reference. In these assays, thrombin-mediated hydrolysis of the chromogenic substrate S2238 (Helena Laboratories, Beaumont, TX) was monitored spectrophotometrically. Addition of an inhibitor to the assay mixture results in decreased absorbance and is indicative of thrombin inhibition. Human thrombin (Enzyme Research Laboratories, Inc., South Bend, IN) at a concentration of 0.2 nM in 0.10 M sodium phosphate buffer, pH 7.5, 0.20 M NaCl, and 0.5% PEG 6000, was incubated with various substrate concentrations ranging from 0.20 to 0.02 mM. After 25 to 30 minutes of incubation, thrombin activity was assayed by monitoring the rate of increase in absorbance at 405 nm that arises owing to substrate hydrolysis. Inhibition constants were derived from reciprocal plots of the reaction velocity as a function of substrate

concentration using the standard method of Lineweaver and Burk. Using the methodology described above, some compounds of this invention were evaluated and found to exhibit a K_i of less than 10 μm, thereby confirming the utility of the compounds of the present invention as effective thrombin inhibitors.

The compounds of the present invention can be administered alone or in combination with one or more additional therapeutic agents. These include other anti-coagulant or coagulation inhibitory agents, anti-platelet or platelet inhibitory agents, thrombin inhibitors, or thrombolytic or fibrinolytic agents.

The compounds are administered to a mammal in a therapeutically effective amount. By "therapeutically effective amount" it is meant an amount of a compound of the present invention that, when administered alone or in combination with an additional therapeutic agent to a mammal, is effective to prevent or ameliorate the thromboembolic disease condition or the progression of the disease.

By "administered in combination" or "combination therapy" it is meant that the compound of the present invention and one or more additional therapeutic agents are administered concurrently to the mammal being treated. When administered in combination each component may be administered at the same time or sequentially in any order at different points in time. Thus, each component may be administered separately but sufficiently closely in time so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in combination with the compounds of this invention include warfarin and heparin, as well as other factor Xa inhibitors such as those described in the publications identified above under Background of the Invention.

The term anti-platelet agents (or platelet inhibitory agents), as used herein, denotes agents that inhibit platelet function such as by inhibiting the aggregation, adhesion or granular secretion of platelets. Such agents include, but are not limited to, the various known non-steroidal anti-inflammatory drugs (NSAIDS) such as aspirin, ibuprofen, naproxen, sulindac, indomethacin, mefenamate, droxicam, diclofenac, sulfinpyrazone, and piroxicam, including pharmaceutically acceptable salts or prodrugs thereof. Of the NSAIDS, aspirin (acetylsalicyclic acid or ASA), and piroxicam are preferred. Other suitable anti-platelet agents include ticlopidine, including pharmaceutically acceptable salts or prodrugs thereof. Ticlopidine is also a preferred compound since it is known to be gentle on the gastro-intestinal tract in use. Still other suitable platelet inhibitory agents include IIb/IIIa antagonists, thromboxane-A2-receptor antagonists and thromboxane-A2-synthetase inhibitors, as well as pharmaceutically acceptable salts or prodrugs thereof.

The term thrombin inhibitors (or anti-thrombin agents), as used herein, denotes inhibitors of the serine protease thrombin. By inhibiting thrombin, various thrombin-mediated processes, such as thrombin-mediated platelet activation (that is, for example, the aggregation of platelets, and/or the granular secretion of plasminogen activator inhibitor-1 and/or serotonin) and/or fibrin formation are disrupted. A number of thrombin inhibitors are known to one of skill in the art and these inhibitors are contemplated to be used in combination with the present compounds. Such inhibitors include, but are not limited to, boroarginine derivatives, boropeptides, heparins, hirudin and argatroban, including pharmaceutically acceptable salts and prodrugs thereof. Boroarginine derivatives and boropeptides include N-acetyl and peptide derivatives of boronic acid, such as C-terminal a-aminoboronic acid derivatives of lysine, ornithine,

arginine, homoarginine and corresponding isothiouronium analogs thereof. The term hirudin, as used herein, includes suitable derivatives or analogs of hirudin, referred to herein as hirulogs, such as disulfatohirudin. Boropeptide thrombin inhibitors include compounds described in Kettner et al., U.S. Patent No. 5,187,157 and European Patent Application Publication Number 293 881 A2, the disclosures of which are hereby incorporated herein by reference. Other suitable boroarginine derivatives and boropeptide thrombin inhibitors include those disclosed in PCT Application Publication Number 92/07869 and European Patent Application Publication Number 471,651 A2, the disclosures of which are hereby incorporated herein by reference.

The term thrombolytics (or fibrinolytic) agents (or thrombolytics or fibrinolytics), as used herein, denotes agents that lyse blood clots (thrombi). Such agents include tissue plasminogen activator, anistreplase, urokinase or streptokinase, including pharmaceutically acceptable salts or prodrugs thereof. The term anistreplase, as used herein, refers to anisoylated plasminogen streptokinase activator complex, as described, for example, in European Patent Application No. 028,489, the disclosure of which is hereby incorporated herein by reference herein. The term urokinase, as used herein, is intended to denote both dual and single chain urokinase, the latter also being referred to herein as prourokinase.

Administration of the compounds of the present invention in combination with such additional therapeutic agent, may afford an efficacy advantage over the compounds and agents alone, and may do so while permitting the use of lower doses of each. A lower dosage minimizes the potential of side effects, thereby providing an increased margin of safety.

The compounds of the present invention are also useful as standard or reference compounds, for example as a quality

standard or control, in tests or assays involving the inhibition of factor Xa. Such compounds may be provided in a commercial kit, for example, for use in pharmaceutical research involving factor Xa. For example, a compound of the present invention could be used as a reference in an assay to compare its known activity to a compound with an unknown activity. This would ensure the experimenter that the assay was being performed properly and provide a basis for comparison, especially if the test compound was a derivative of the reference compound. When developing new assays or protocols, compounds according to the present invention could be used to test their effectiveness.

The compounds of the present invention may also be used in diagnostic assays involving factor Xa. For example, the presence of factor Xa in an unknown sample could be determined by addition of chromogenic substrate S2222 to a series of solutions containing test sample and optionally one of the compounds of the present invention. If production of pNA is observed in the solutions containing test sample, but not in the presence of a compound of the present invention, then one would conclude factor Xa was present.

Dosage and Formulation

The compounds of this invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions. They may also be administered in intravenous (bolus or infusion), intraperitoneal, subcutaneous, or intramuscular form, all using dosage forms well known to those of ordinary skill in the pharmaceutical arts. They can be administered alone, but generally will be administered with a pharmaceutical

carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage regimen for the compounds of the present invention will, of course, vary depending upon known factors, such as the pharmacodynamic characteristics of the particular agent and its mode and route of administration; the species, age, sex, health, medical condition, and weight of the recipient; the nature and extent of the symptoms; the kind of concurrent treatment; the frequency of treatment; the route of administration, the renal and hepatic function of the patient,and the effect desired. A physician or veterinarian can determine and prescribe the effective amount of the drug required to prevent, counter, or arrest the progress of the thromboembolic disorder.

By way of general guidance, the daily oral dosage of each active ingredient, when used for the indicated effects, will range between about 0.001 to 1000 mg/kg of body weight, preferably between about 0.01 to 100 mg/kg of body weight per day, and most preferably between about 1.0 to 20 mg/kg/day. Intravenously, the most preferred doses will range from about 1 to about 10 mg/kg/minute during a constant rate infusion. Compounds of this invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three, or four times daily.

Compounds of this invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal routes, using transdermal skin patches. When administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

The compounds are typically administered in admixture with suitable pharmaceutical diluents, excipients, or carriers (collectively referred to herein as pharmaceutical

carriers) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules, elixirs, syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic, pharmaceutically acceptable, inert carrier such as lactose, starch, sucrose, glucose, methyl callulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol and the like; for oral administration in liquid form, the oral drug components can be combined with any oral, non-toxic, pharmaceutically acceptable inert carrier such as ethanol, glycerol, water, and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents, and coloring agents can also be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars such as glucose or beta-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth, or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum, and the like.

The compounds of the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine, or phosphatidylcholines.

Compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer,

polyhydroxypropylmethacrylamide-phenol, polyhydroxyethylaspartamidephenol, or polyethyleneoxide-polylysine substituted with palmitoyl residues. Furthermore, the compounds of the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacylates, and crosslinked or amphipathic block copolymers of hydrogels.

Dosage forms (pharmaceutical compositions) suitable for administration may contain from about 1 milligram to about 100 milligrams of active ingredient per dosage unit. In these pharmaceutical compositions the active ingredient will ordinarily be present in an amount of about 0.5-95% by weight based on the total weight of the composition.

Gelatin capsules may contain the active ingredient and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric coated for selective disintegration in the gastrointestinal tract.

Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance.

In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble

salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium EDTA. In addition, parenteral solutions can contain preservatives, such as benzalkonium chloride, methyl- or propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, Mack Publishing Company, a standard reference text in this field.

Representative useful pharmaceutical dosage-forms for administration of the compounds of this invention can be illustrated as follows:

Capsules

A large number of unit capsules can be prepared by filling standard two-piece hard gelatin capsules each with 100 milligrams of powdered active ingredient, 150 milligrams of lactose, 50 milligrams of cellulose, and 6 milligrams magnesium stearate.

Soft Gelatin Capsules

A mixture of active ingredient in a digestable oil such as soybean oil, cottonseed oil or olive oil may be prepared and injected by means of a positive displacement pump into gelatin to form soft gelatin capsules containing 100 milligrams of the active ingredient. The capsules should be washed and dried.

Tablets

Tablets may be prepared by conventional procedures so that the dosage unit is 100 milligrams of active ingredient, 0.2 milligrams of colloidal silicon dioxide, 5 milligrams of magnesium stearate, 275 milligrams of microcrystalline cellulose, 11 milligrams of starch and 98.8 milligrams of lactose. Appropriate coatings may be applied to increase palatability or delay absorption.

Injectable

A parenteral composition suitable for administration by injection may be prepared by stirring 1.5% by weight of active ingredient in 10% by volume propylene glycol and water. The solution should be made isotonic with sodium chloride and sterilized.

Suspension

An aqueous suspension can be prepared for oral administration so that each 5 mL contain 100 mg of finely divided active ingredient, 200 mg of sodium carboxymethyl cellulose, 5 mg of sodium benzoate, 1.0 g of sorbitol solution, U.S.P., and 0.025 mL of vanillin.

Where the compounds of this invention are combined with other anticoagulant agents, for example, a daily dosage may be about 0.1 to 100 milligrams of the compound of the present invention and about 1 to 7.5 milligrams of the second anticoagulant, per kilogram of patient body weight. For a tablet dosage form, the compounds of this invention generally may be present in an amount of about 5 to 10 milligrams per dosage unit, and the second anti-coagulant in an amount of about 1 to 5 milligrams per dosage unit.

Where the compounds of the present invention are administered in combination with an anti-platelet agent, by way of general guidance, typically a daily dosage may be about 0.01 to 25 milligrams of the compound of the present invention and about 50 to 150 milligrams of the anti-platelet agent, preferably about 0.1 to 1 milligrams of the compound of the present invention and about 1 to 3 milligrams of anti-platelet agents, per kilogram of patient body weight.

Where the compounds of the present invention are adminstered in combination with thrombolytic agent, typically a daily dosage may be about 0.1 to 1 milligrams of the compound of the present invention, per kilogram of patient body weight and, in the case of the thrombolytic

agents, the usual dosage of the thrombolyic agent when administered alone may be reduced by about 70-80% when administered with a compound of the present invention.

Where two or more of the foregoing second therapeutic agents are administered with the compound of the present invention, generally the amount of each component in a typical daily dosage and typical dosage form may be reduced relative to the usual dosage of the agent when administered alone, in view of the additive or synergistic effect of the therapeutic agents when administered in combination.

Particularly when provided as a single dosage unit, the potential exists for a chemical interaction between the combined active ingredients. For this reason, when the compound of the present invention and a second therapeutic agent are combined in a single dosage unit they are formulated such that although the active ingredients are combined in a single dosage unit, the physical contact between the active ingredients is minimized (that is, reduced). For example, one active ingredient may be enteric coated. By enteric coating one of the active ingredients, it is possible not only to minimize the contact between the combined active ingredients, but also, it is possible to control the release of one of these components in the gastrointestinal tract such that one of these components is not released in the stomach but rather is released in the intestines. One of the active ingredients may also be coated with a material that effects a sustained-release throughout the gastrointestinal tract and also serves to minimize physical contact between the combined active ingredients. Furthermore, the sustained-released component can be additionally enteric coated such that the release of this component occurs only in the intestine. Still another approach would involve the formulation of a combination product in which the one component is coated with a sustained and/or enteric release polymer, and the other

component is also coated with a polymer such as a low-viscosity grade of hydroxypropyl methylcellulose (HPMC) or other appropriate materials as known in the art, in order to further separate the active components. The polymer coating serves to form an additional barrier to interaction with the other component.

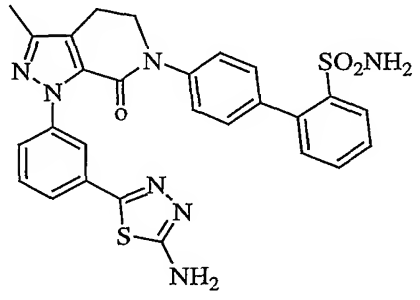
These as well as other ways of minimizing contact between the components of combination products of the present invention, whether administered in a single dosage form or administered in separate forms but at the same time by the same manner, will be readily apparent to those skilled in the art, once armed with the present disclosure.

Other features of the invention will become apparent in the course of the following descriptions of exemplary embodiments that are given for illustration of the invention and are not intended to be limiting thereof.

EXAMPLES

Example 1

1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-methyl-6-[2'-aminosulfonyl-[1,1']-biphen-4-yl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one trifluoroacetic acid salt



Part A: 1-[4-bromophenyl]-4-acetyl-2,3-dioxopiperidine was prepared in four steps in 10% overall yield by the following sequence of reactions. Commercially available 4-bromoaniline was treated with commercially available 5-chloro-2-pentanone ethylene ketal in dimethylformamide in the presence of potassium carbonate for three days. The

crude alkylated aniline was treated with ethyloxalyl chloride in THF the presence of triethylamine. Hydrolysis of the ketal was accomplished by treating with aqueous HCl and the resulting material was subjected to Dieckmann cyclization conditions (NaOMe, methanol). The crude dioxopiperidine was purified by flash chromatography (elution with 4:1 hexanes/ethylacetate) to afford the title compound. ^{1}H NMR (dmso d6): δ 7.56 (d, 2H, J = 8Hz), 7.26 (d, 2H, J = 8Hz), 3.60 (t, 2H), 3.28 (t, 2H), 2.30 (s, 3H). LRMS (ES+): 281.0 $(M+H)^+$.

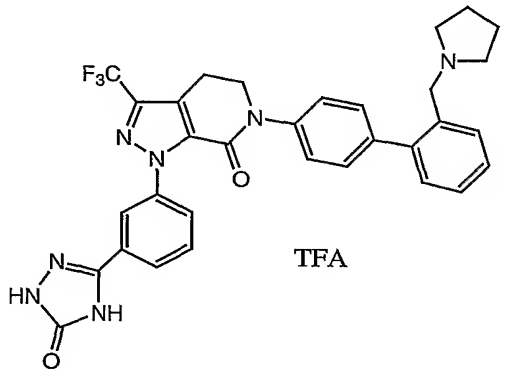
Part B: 1-[3-Cyanophenyl]-3-methyl-6-[2'-aminosulfonyl-[1,1']-biphen-4-yl]-1,4,5,6-tetrahydropyrazolo-[3,4-*c*]-pyridin-7-one was prepared by addition of 3-cyanophenyl hydrazine to a solution of 1-[4-bromophenyl]-4-acetyl-2,3-dioxopiperidine in glacial acetic acid was added. The reaction mixture was stirred at reflux for 3 h and then was cooled to ambient temperature. The volatiles were removed and the residue was taken up in ethyl acetate. The organics were washed with saturated aq sodium bicarbonate and brine, dried ($MgSO_4$) and concentrated.

The residue was dissolved in benzene and then there was added tetrabutylammonium bromide, aqueous Na_2CO_3 and 2-(*tert*-butylaminosulfonyl)phenylboronic. This solution was degassed with a stream of nitrogen for 30 minutes. Following the purge, tetrakis(triphenylphosphine)palladium(0) was added and the solution was stirred overnight at reflux. The solution was diluted with EtOAc and washed twice with brine and the organics dried over $MgSO_4$, filtered and the volatiles removed under reduced pressure. The residue was purified by column chromatography (elution with 1:1 hexane/EtOAc) to afford an intermediate biphenyl compound.

Part C: 1-[3-Cyanophenyl]-3-methyl-6-[2'-aminosulfonyl-[1,1']-biphen-4-yl]-1,4,5,6-tetrahydropyrazolo-[3,4-*c*]-pyridin-7-one was (0.12 g, 0.22 mmol) was treated with thiosemicarbazide (0.02 g, 0.22 mmol) in 10 mL refluxing TFA for 4H. The reaction mixture was concentrated under reduced pressure and purified by HPLC to give the aminothiadiazole. ^{1}H NMR (DMSO-d_6, 300MHz) δ: 8.04 (d, 2H, J=7Hz), 7.72-7.51 (m, 7H), 7.33 (d, 1H, J=7Hz), 7.26 (s, 2H), 4.15-4.13 (m, 2H), 2.96 (bt, 2H, J=6Hz), 2.31 (s, 3H) ppm; LRMS: m/z 558 (M+H); HRMS: calc'd for C_{27} H_{24} S_2 O_3 N_7=558.4216.

Example 2

1-[3-(5-oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-c]pyridin-7-one, trifluoroacetic acid salt



Part A: Preparation of 1-(4-iodophenyl)-4-(2,2,2-trifluoropropanoyl)-2,3-piperidinedione

4-Iodoaniline (45.82 g, 209.2 m mol) and triethylamine (65.61 mL, 470.7 m mol) were dissolved into THF (800 mL) and cooled to 0^{0}C. 5-Bromovaleryl chloride (50.0 g, 251.1 m mol) dissolved in THF (200 mL) was added dropwise to the reaction. The reaction was warmed to room temperature and stirred overnight. Reaction was cooled to 0^{0}C and potassium

tert-butoxide (70.43 g, 627.6 m mol) was slowly added. The reaction was warmed to room temperature and stirred overnight. The reaction was concentrated and then redissolved in ethyl acetate (500 mL) and 3N HCl (500 mL), extracted with ethyl acetate (2x250 mL), washed with 1N HCl (3x250 mL), washed with brine (1x250 mL), and dried (Na_2SO_4). Purification by silica gel chromatography using 0%-100%ethyl acetate/hexane gradient as eluent to afford 51.03g (81%): ^1H NMR ($CDCl_3$)δ 7.70(d, J=8.4Hz, 2H), 7.03(d, J=8.8Hz, 2H), 3.62(t, J=5.9Hz, 2H), 2.56(t, J=5.7Hz, 2H), 2.50-1.88(m,4H)ppm.

The product from the above reaction (85.17 g, 282.8 m mol) and phosphorus pentachloride (205.91 g, 990.0 m mol) was dissolved into $CHCl_3$ (750 mL) and refluxed for 3½ hours. The reaction was poured over ice and then quenched further with water, extracted with $CHCl_3$ (3x400 mL), washed with brine (1x400 mL), dried ($MgSO_4$), and concentrated. This residue was dissolved in morpholine (400 mL) and refluxed overnight. The reaction was concentrated and purified by silica gel chromatography using 0%-100% ethyl acetate/hexane gradient as eluent to afford 68 g (63%) of desired morpholine adduct: ^1H NMR ($CDCl_3$)δ 7.68(d, J=8.8Hz, 2H), 7.11(d, J=8.8Hz, 2H), 5.66(t, J=4.8Hz, 1H), 3.82(t, J=4.8Hz, 4H), 3.77(t, J=6.8Hz, 2H), 2.89(t, J=4.8Hz, 4H), 2.53-2.47(m, 2H)ppm.

4-Dimethylaminopyridine (3.92 g, 32.01 m mol) was dissolved into CH_2Cl_2 (130 mL) and cooled to 0^0C. Trifluoroacetic anhydride (4.54 g, 32.01 m mol) was added and the mixture was stirred at 0^0C for 30 min. The above morpholine-enamine (10.25 g, 26.68 m mol) dissolved in CH_2Cl_2 (370 mL) was added slowly and the reaction was warmed to room temperature and stirred overnight. Reaction was concentrated and purified by silica gel chromatography using 0%-50% ethylacetate/hexane gradient to isolate the intermediate.

The intermediate was dissolved in 20% HCl (50 mL) and diethyl ether (200 mL) and stirred at room temperature overnight. Reaction was quenched with water, extracted with ether (3x100 mL), washed with brine (1x100 mL), and dried (Na_2SO_4). The residue was redissolved in petroleum ether and the solids were filtered away. Concentrated filtrate afforded 9.99 g (78%) of the desired compound: ^1H NMR ($CDCl_3$)δ 7.77(d, J=8.8Hz, 2H), 7.11(d, J=8.8Hz, 2H), 3.93(t, J=6.8Hz, 2H), 2.92(t, J=6.8Hz, 2H)ppm.

Part B: Preparation of 1-(3-cyanophenyl)-3-(trifluoromethyl)-6-(4-iodophenyl)-1,4,5,6-tetrahydropyrazolo-[3,4-*c*]-pyridin-7-one

1-(4-iodophenyl)-4-(2,2,2-trifluoroacetyl)-2,3-piperidinedione prepared by the same methods described in WO 00/39131 (5.02 g, 12.2 mmol) and 3-cyanophenylhydrazine chloride (3.44 g, 20.4 mmol) were added together with 75 mL of Acetic acid. The mixture was refluxed for 4 hours. The mixture was cooled and the solvent was removed. The residue was partitioned between EtOAc and H_2O. The EtOAc layer was washed with H_2O, brine, dried over $MgSO_4$, concentrated, and chromatographed with 1:5 EtOAc:hexane to afford 3.8 g of 1-(3-cyanophenyl)-3-(trifluoromethyl)-6-(4-iodophenyl)-1,4,5,6-tetrahydropyrazolo-[3,4-*c*]-pyridin-7-one as a yellow solid (61.3%). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.91-7.90 (m, 1H), 7.87-7.83 (m, 1H), 7.75-7.69 (m, 3H), 7.56 (t, 1H), 7.09-7.04 (m, 2H), 4.15 (t, 2H), 3.19 (t, 2H).

Part C: Preparation of 1-[3-(5-oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[(4-iodophenyl)]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one

1-(3-Cyanophenyl)-3-(trifluoromethyl)-6-(4-iodophenyl)-1,4,5,6-tetrahydropyrazolo-[3,4-*c*]-pyridin-7-one (3.75 g, 7.38 mmol) was suspended in 100 mL of anhydrous MeOH and 50

mL of chloroform and cooled in a 0°C ice-bath. HCl gas was then bubbled in the mixture for 30 minutes resulting in a clear solution. The reaction vessel was sealed and stored at 0°C for 18 hours. The mixture was concentrated in vacuo and dried. The resulting yellow was suspended in 75 mL of anhydrous 1,4-dioxane. Semicarbazide hydrochloride (1.41 g, 12.6 mmol) was then added, followed by N-methylmorpholine (5.83 mL, 53 mmol). The mixture was refluxed for 48 hours. The precipitate was filtered and washed with 1,4-dioxane, water, and ether. The solid was pumped dry to afford 1.7g of the title compound as a yellow solid (40.7%). MS (ES^-): 565.2, $(M-H)^-$.

Part D: Preparation of 1-[3-(5-oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-formyl-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one

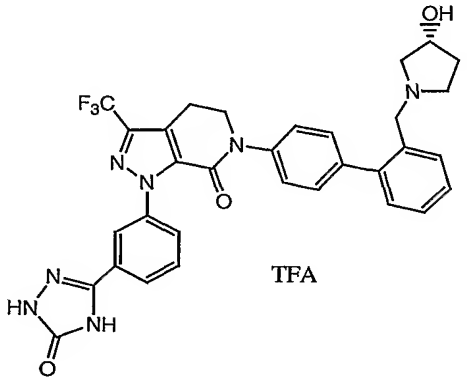
1-[3-(5-Oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[(4-iodophenyl)]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one (300 mg, 0.53 mmol), 2-Formylbenzeneboronic acid (159 mg, 1.06 mmol), K_2CO_3 (293 mg, 2.12 mmol), were dissolved in 15 mL of 1:2 EtOH:Toluene. The system was evacuated and flushed with N_2 three times. $Pd(PPh_3)_4$ (61 mg, 0.053 mmol) was then added and the system was evacuated and flushed with N_2 three times. The mixture was refluxed for seven hours. The mixture was concentrated in vacuo and the residue partitioned between ethyl acetate and H_2O. The aqueous layer was extracted with more ethyl acetate (2 x 50 mL). The ethyl acetate layers were combined and washed with brine. The aqueous layer was extracted with CH_2Cl_2. All organic layers were combined and dried over $MgSO_4$, concentrated and chromatographed with 1% to 4% MeOH:$CHCl_3$ to afford 170 mg of the title compound as an off-white solid (58.9%). MS (ES^+): 545.3, $(M+H)^+$.

Part E: Preparation of 1-[3-(5-oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, trifluoroacetic acid salt

1-[3-(5-Oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-formyl-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one (82 mg, 0.15 mmol) and pyrrolidine (32 mg, 0.45 mmol) were dissolved in 10 mL of methanol and stirred at room temperature for 18 hours. Sodium cyanoborohydride (19 mg, 0.3 mmol) was then added and the mixture was stirred at room temperature for 3 hours. The mixture was concentrated in vacuo and purified by reverse phase HPLC (C18 reverse phase column, eluted with a H_2O/CH_3CN gradient with 0.05% TFA) to give 40 mg of the title compound as a white solid (37.4% yield). LRMS (ES^+), 600.4 $(M+H)^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 12.11(s, 1H), 11.77 (s, 1H), 7.99 (s, 1H), 7.85 (d, 1H), 7.69-7.66 (m, 2H), 7.61-7.55 (m, 1H), 7.48-7.46 (m, 4H), 7.37 (d, 2H), 7.32-7.29 (m, 1H), 4.35 (s, 1H), 4.17 (t, 2H), 3.35-3.25 (m, 2H), 3.14 (t, 2H), 2.85-2.75 (m, 2H), 1.8-1.7 (m, 4H).

Example 3

6-(2'-{[(3*S*)-3-Hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, trifluoroacetic acid salt

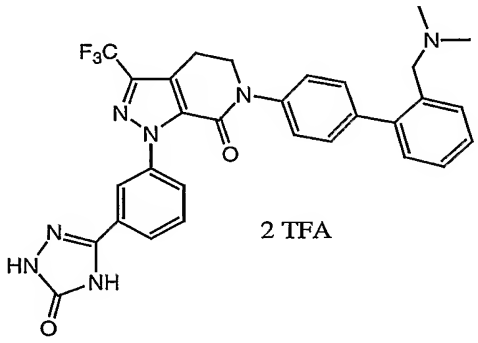


TFA

This compound was prepared by the methods described in Example 2. LRMS (ES^+), 616.5 $(M+H)^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 12.1(s, 1H), 11.75 (s, 1H), 7.99 (s, 1H), 7.85-7.83 (m, 1H), 7.75-7.67 (m, 2H), 7.58-7.42 (m, 5H), 7.37-7.25 (m, 3H), 4.45-4.2 (m, 3H), 4.2-4.15 (m, 2H), 3.2-3.1 (m, 2H), 2.9-2.75 (m, 4H), 1.87-1.65 (m, 2H).

Example 4

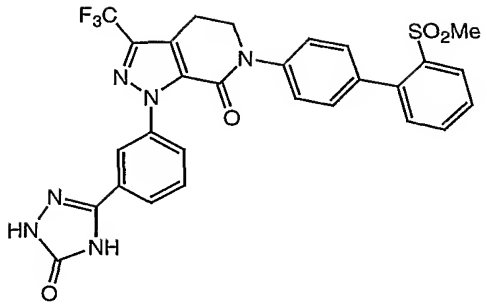
6-{2'-[(Dimethylamino)methyl]-1,1'-biphenyl-4-yl}-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, bistrifluoroacetic acid salt



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 574.4$(M+H)^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 12.11(s, 1H), 11.77 (s, 1H), 7.99 (s, 1H), 7.85 (d, 1H), 7.70-7.65 (m, 2H), 7.61-7.56 (m, 1H), 7.51-7.45 (m, 4H), 7.37-7.29 (m, 3H), 4.27(bs, 2H), 4.18 (t, 2H), 3.14 (t, 2H), 2.45 (s, 6H).

Example 5

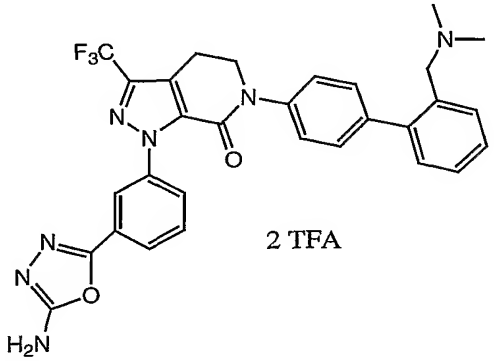
6-[2'-(Methylsulfonyl)-1,1'-biphenyl-4-yl]-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 617.5 $(M+H)^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 12.1(s, 1H), 11.76 (s, 1H), 8.07-8.05 (m, 1H), 7.99 (s, 1H), 7.85 (d, 1H), 7.75-7.58 (m, 4H), 7.41-7.35 (m, 5H), 4.18 (t, 2H), 3.14 (t, 2H), 2.81 (s, 3H).

Example 6

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-6-{2'-[(dimethylamino)methyl]-1,1'-biphenyl-4-yl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, bistrifluoroacetic acid salt

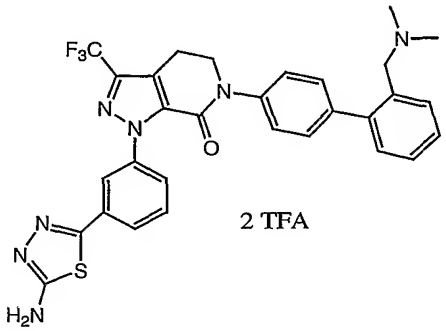


This compound was prepared by the methods described in Example 2. LRMS (ES^+), 574.4 $(M+H)^+$. ^1H NMR (CD_3OD, 300 MHz) δ 8.12 (s, 1H), 7.97 (d, 1H), 7.78-7.75 (m, 1H), 7.66-7.39 (m, 6H), 7.42-7.36 (m, 3H), 4.34 (s, 2H), 4.24 (t, 2H), 3.30-3.21 (m, 2H), 2.60 (s, 6H).

Example 7

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-{2'-[(dimethylamino)methyl]-1,1'-biphenyl-4-yl}-3-

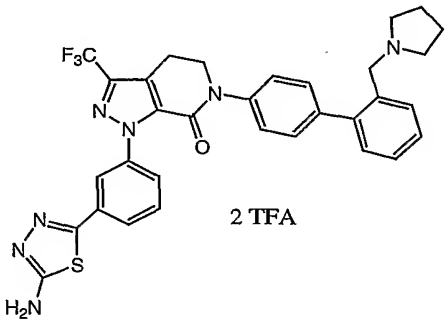
(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, bistrifluoroacetic acid salt



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 590.5$(M+H)^+$. ^1H NMR (CD_3OD, 300 MHz) δ 8.09 (s, 1H), 7.9-7.85 (m, 1H), 7.75-7.7 (m, 1H), 7.65-7.5 (m, 6H), 7.4-7.35 (m, 3H), 4.36 (s, 2H), 4.26 (t, 2H), 3.25 (t, 2H), 2.62 (s, 6H).

Example 8

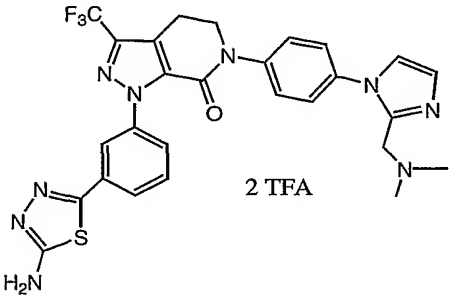
1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, bistrifluoroacetic acid salt



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 616.5 $(M+H)^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 8.01 (t, 1H), 7.81-7.78 (m, 1H), 7.69-7.63 (m, 2H), 7.59-7.45 (m, 5H), 7.38-7.29 (m, 3H), 4.35-4.33 (m, 2H), 4.18 (t, 2H), 3.35-3.22 (m, 2H), 3.14 (t, 2H), 2.81-2.72 (m, 2H), 1.8 -1.68 (m, 4H).

Example 9

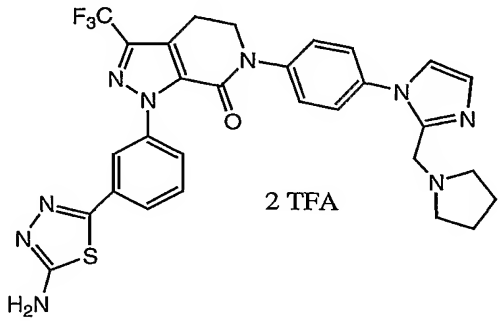
1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-(4-{2-[(dimethylamino)methyl]-1*H*-imidazol-1-yl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, bistrifluoroacetic acid salt



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 580.4$(M+H)^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 8.02-8.01 (m, 1H), 7.79-7.76 (m, 1H), 7.66-7.64 (m, 1H), 7.58-7.48 (m, 6H), 7.21-7.20 (m, 1H), 4.39 (s, 2H), 4.16 (t, 2H), 3.14 (t, 2H), 2.75 (s, 6H).

Example 10

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-{4-[2-(1-pyrrolidinylmethyl)-1*H*-imidazol-1-yl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, bistrifluoroacetic acid salt

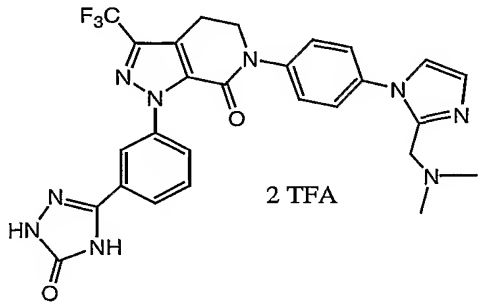


This compound was prepared by the methods described in Example 2. LRMS (ES^+), 606.6 $(M+H)^+$. ^1H NMR (CD_3OD, 300 MHz) δ 8.06 (s, 1H), 7.88-7.82 (m, 1H), 7.7-7.65 (m, 1H), 7.61-7.58 (m, 3H), 7.49 (d, 2H), 7.40 (d, 1H), 7.22 (s, 1H), 4.46

(s, 2H), 4.23 (t, 2H), 3.4 -3.3 (m, 4H), 3.22 (t, 2H), 2.03-1.98 (m, 4H).

Example 11

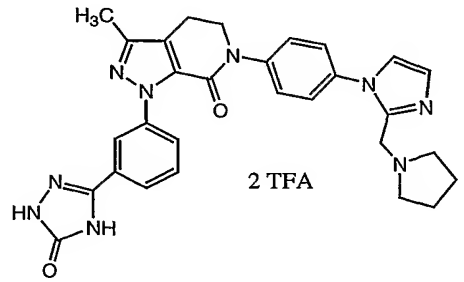
6-(4-{2-[(Dimethylamino)methyl]-1*H*-imidazol-1-yl}phenyl)-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, bistrifluoroacetic acid salt



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 546.5 $(M+H)^+$. ^1H NMR (DMSO-d_6, 300 MHz) δ 8.0 (s, 1H), 7.85-7.81 (m, 1H), 7.7-7.65 (m, 1H), 7.6-7.5 (m, 6H), 7.2 (s, 1H), 4.4 (s, 2H), 4.19-4.15 (m, 2H), 3.18-3.13 (m, 2H), 2.76 (s, 6H).

Example 12

3-Methyl-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-{4-[2-(1-pyrrolidinylmethyl)-1*H*-imidazol-1-yl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, trifluoroacetic acid salt

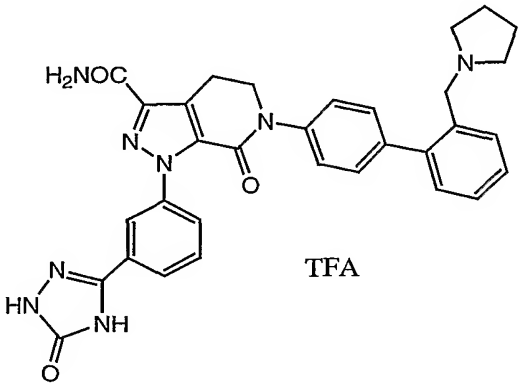


This compound was prepared by the methods described in Example 2. LRMS (ES^+), 546.5 $(M+H)^+$. ^1H NMR (CD_3OD, 300 MHz)

δ 7.98 (t, 1H), 7.81 (d, 1H), 7.68-7.64 (m, 2H), 7.56-7.49 (m, 5H), 7.41-7.38 (m, 3H), 4.42 (s, 2H), 4.21 (t, 2H), 3.4-3.3(m, 2H), 3.05 (t, 2H), 2.88-2.78 (m, 2H), 2.37 (s, 3H), 1.93-1.84 (m, 4H).

Example 13

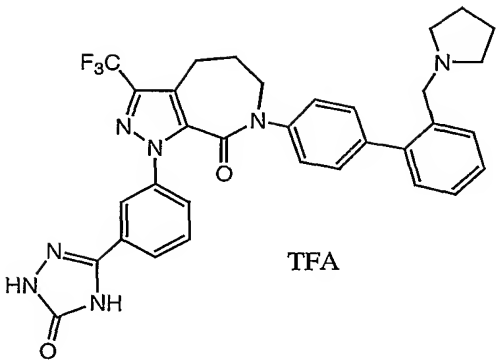
7-Oxo-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide, trifluoroacetic acid salt



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 575.6 $(M+H)^+$. ^1H NMR (CD_3OD, 300 MHz) δ 8.06-8.05 (m, 1H), 7.88-7.84 (m, 1H), 7.78-7.74 (m, 1H), 7.61-7.45 (m, 6H), 7.4-7.35 (m, 3H), 4.41 (s, 2H), 4.21 (t, 2H), 3.4-3.3 (m, 4H), 2.82-2.78 (m, 2H), 1.9-1.82 (m, 4H).

Example 14

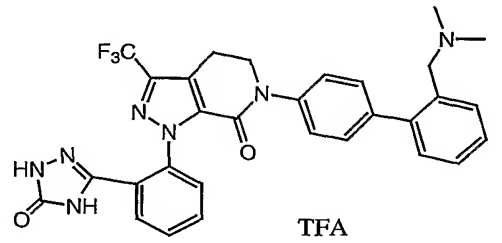
1-[3-(5-Oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-7-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[3,4-*c*]azepin-8(1*H*)-one, trifluoroacetic acid salt



This compound was prepared by the methods described in Example 2. LRMS (ES^+), 632.6 $(M+H)^+$. ^1H NMR (CD_3OD, 300 MHz) δ 7.96-7.95 (m, 1H), 7.88-7.84 (m, 1H), 7.65-7.53 (m, 6H), 7.41-7.38 (m, 1H), 7.31-7.23 (m, 2H), 4.4 (s, 2H), 4.05-4.01 (m, 2H), 3.35-3.29 (m, 2H), 3.13 (t, 2H), 2.84-2.81 (m, 2H), 2.33-2.30 (m, 2H), 1.93-1.85 (m, 4H).

Example 15

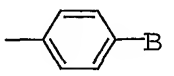
1-[2-(5-Oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one, trifluoroacetic acid salt



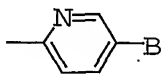
This compound was prepared by the methods described in Example 2. LRMS (ES^+), 574.5$(M+H)^+$. ^1H NMR (CD_3OD, 300 MHz) δ 7.71-7.53 (m, 6H), 7.43-7.35 (m, 6H), 4.34 (s, 2H), 4.16 (t, 2H), 3.21 (t, 2H), 2.61 (s, 6H).

The following tables contain representative examples of the present invention. Each entry in each table is intended to be paired with each formulas at the start of the table. For example, in Table 1, Example 1 is intended to be paired with each of the formulas.

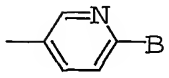
The following nomenclature is intended for group A in the following tables.



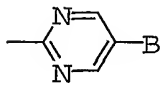
phenyl



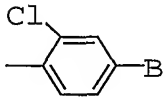
2-pyridyl



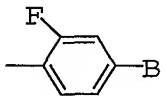
3-pyridyl



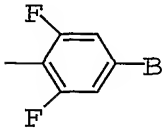
2-pyrimidyl



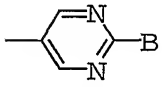
2-Cl-phenyl



2-F-phenyl

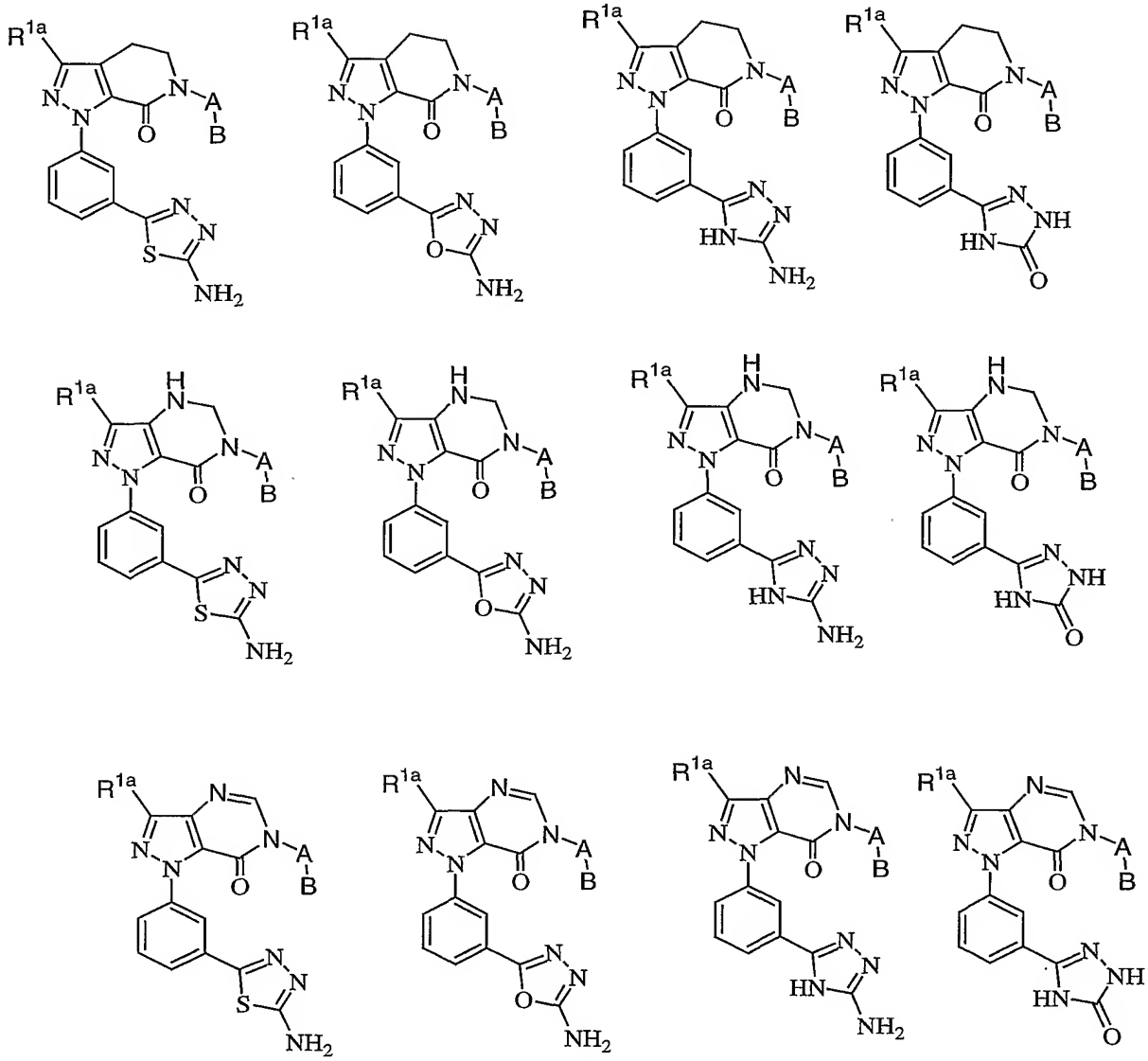


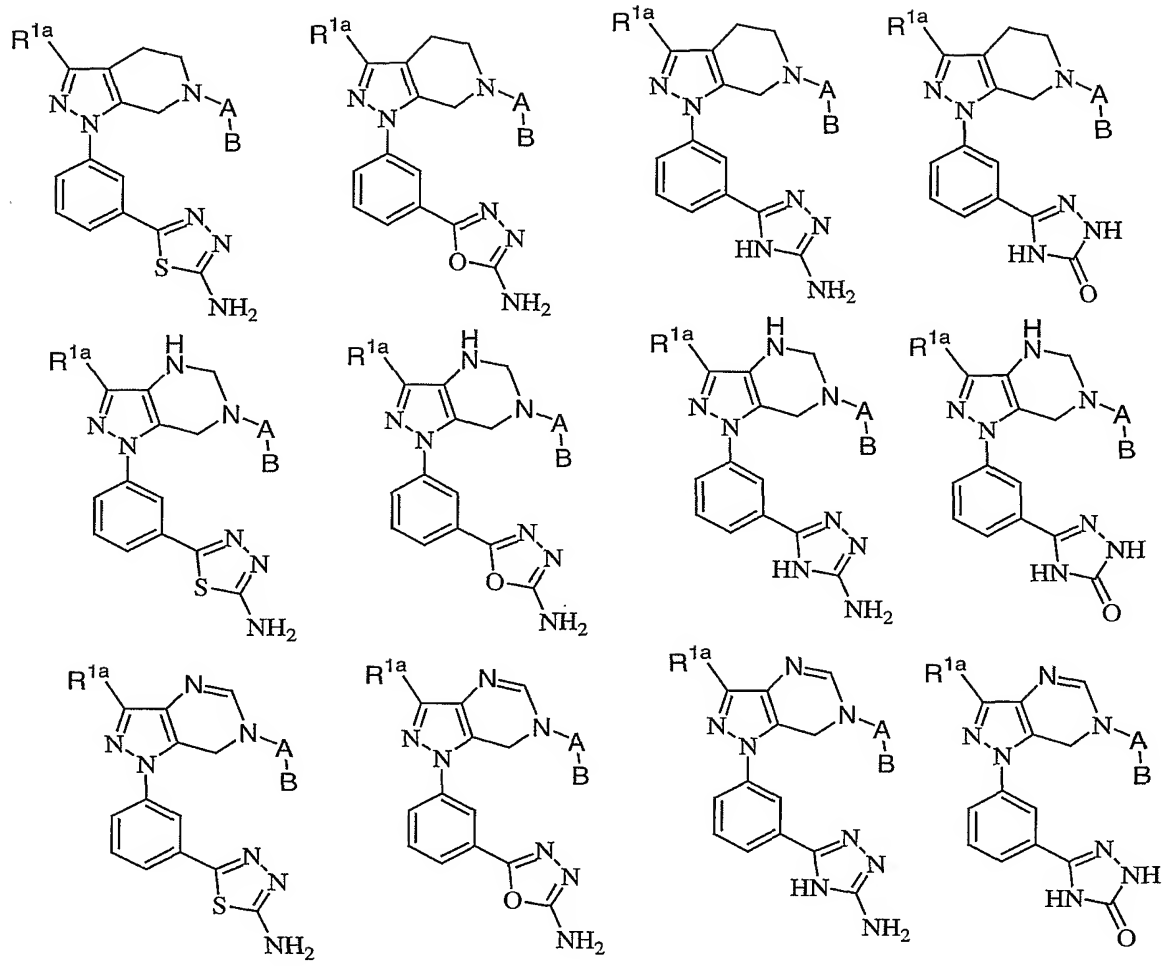
2,6-diF-phenyl



5-pyrimidyl

Table 1





R^{1a} is CH_3;

Ex#	A	B
1.	phenyl	2-(NH_2SO_2)phenyl
2.	phenyl	2-(CH_3SO_2)phenyl
3.	phenyl	3-NH_2SO_2-4-pyridyl
4.	phenyl	3-CH_3SO_2-4-pyridyl
5.	phenyl	2-(CH_3NH)phenyl
6.	phenyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
7.	phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
8.	phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
9.	phenyl	2-((CH_3)$_2NCH_2$)phenyl
10.	phenyl	2-((CH_3)$NHCH_2$)phenyl
11.	phenyl	2-((CH_3CH_2)$NHCH_2$)phenyl
12.	phenyl	2-((CH_3CH_2)$_2NCH_2$)phenyl
13.	phenyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
14.	phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
15.	phenyl	2-(((CH_3)$_2$CH)$_2NCH_2$)phenyl
16.	phenyl	2-((cyclopropyl)$NHCH_2$)phenyl
17.	phenyl	2-((cyclopropyl)$_2NCH_2$)phenyl

18.	phenyl	2-((cyclobutyl)$NHCH_2$)phenyl
19.	phenyl	2-((cyclobutyl)$_2NCH_2$)phenyl
20.	phenyl	2-((cyclopentyl)$NHCH_2$)phenyl
21.	phenyl	2-((cyclopentyl)$_2NCH_2$)phenyl
22.	phenyl	2-((cyclohexyl)$NHCH_2$)phenyl
23.	phenyl	2-((cyclohexyl)$_2NCH_2$)phenyl
24.	phenyl	1-CH_3-2-imidazolyl
25.	phenyl	2-CH_3-1-imidazolyl
26.	phenyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
27.	phenyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
28.	phenyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
29.	phenyl	2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
30.	phenyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
31.	phenyl	2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
32.	phenyl	2-(((CH_3)$_2$CH)$_2NCH_2$)-1-imidazolyl
33.	phenyl	2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
34.	phenyl	2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
35.	phenyl	2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
36.	phenyl	2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
37.	phenyl	2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
38.	phenyl	2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
39.	phenyl	2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
40.	phenyl	2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
41.	2-pyridyl	2-(NH_2SO_2)phenyl
42.	2-pyridyl	2-(CH_3SO_2)phenyl
43.	2-pyridyl	3-NH_2SO_2-4-pyridyl
44.	2-pyridyl	3-CH_3SO_2-4-pyridyl
45.	2-pyridyl	2-(CH_3NH)phenyl
46.	2-pyridyl	3-((CH_3)$_2NCH_2$)-4-pyridyl
47.	2-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
48.	2-pyridyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
49.	2-pyridyl	2-((CH_3)$_2NCH_2$)phenyl
50.	2-pyridyl	2-((CH_3)$NHCH_2$)phenyl
51.	2-pyridyl	2-((CH_3CH_2)$NHCH_2$)phenyl
52.	2-pyridyl	2-((CH_3CH_2)$_2NCH_2$)phenyl
53.	2-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
54.	2-pyridyl	2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
55.	2-pyridyl	2-(((CH_3)$_2$CH)$_2NCH_2$)phenyl
56.	2-pyridyl	2-((cyclopropyl)$NHCH_2$)phenyl
57.	2-pyridyl	2-((cyclopropyl)$_2NCH_2$)phenyl
58.	2-pyridyl	2-((cyclobutyl)$NHCH_2$)phenyl
59.	2-pyridyl	2-((cyclobutyl)$_2NCH_2$)phenyl
60.	2-pyridyl	2-((cyclopentyl)$NHCH_2$)phenyl
61.	2-pyridyl	2-((cyclopentyl)$_2NCH_2$)phenyl
62.	2-pyridyl	2-((cyclohexyl)$NHCH_2$)phenyl
63.	2-pyridyl	2-((cyclohexyl)$_2NCH_2$)phenyl
64.	2-pyridyl	1-CH_3-2-imidazolyl
65.	2-pyridyl	2-CH_3-1-imidazolyl
66.	2-pyridyl	2-((CH_3)$_2NCH_2$)-1-imidazolyl
67.	2-pyridyl	2-((CH_3)$NHCH_2$)-1-imidazolyl
68.	2-pyridyl	2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
69.	2-pyridyl	2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
70.	2-pyridyl	2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl

71.	2-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
72.	2-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
73.	2-pyridyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
74.	2-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
75.	2-pyridyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
76.	2-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
77.	2-pyridyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
78.	2-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
79.	2-pyridyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
80.	2-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
81.	3-pyridyl	2-(NH$_2$SO$_2$)phenyl
82.	3-pyridyl	2-(CH$_3$SO$_2$)phenyl
83.	3-pyridyl	3-NH$_2$SO$_2$-4-pyridyl
84.	3-pyridyl	3-CH$_3$SO$_2$-4-pyridyl
85.	3-pyridyl	2-(CH$_3$NH)phenyl
86.	3-pyridyl	3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
87.	3-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
88.	3-pyridyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
89.	3-pyridyl	2-((CH$_3$)$_2$NCH$_2$)phenyl
90.	3-pyridyl	2-((CH$_3$)NHCH$_2$)phenyl
91.	3-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
92.	3-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
93.	3-pyridyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
94.	3-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
95.	3-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
96.	3-pyridyl	2-((cyclopropyl)NHCH$_2$)phenyl
97.	3-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
98.	3-pyridyl	2-((cyclobutyl)NHCH$_2$)phenyl
99.	3-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
100.	3-pyridyl	2-((cyclopentyl)NHCH$_2$)phenyl
101.	3-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
102.	3-pyridyl	2-((cyclohexyl)NHCH$_2$)phenyl
103.	3-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
104.	3-pyridyl	1-CH$_3$-2-imidazolyl
105.	3-pyridyl	2-CH$_3$-1-imidazolyl
106.	3-pyridyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
107.	3-pyridyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
108.	3-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
109.	3-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
110.	3-pyridyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
111.	3-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
112.	3-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
113.	3-pyridyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
114.	3-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
115.	3-pyridyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
116.	3-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
117.	3-pyridyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
118.	3-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
119.	3-pyridyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
120.	3-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
121.	2-pyrimidyl	2-(NH$_2$SO$_2$)phenyl
122.	2-pyrimidyl	2-(CH$_3$SO$_2$)phenyl
123.	2-pyrimidyl	3-NH$_2$SO$_2$-4-pyridyl

124. 2-pyrimidyl 3-CH_3SO_2-4-pyridyl
125. 2-pyrimidyl 2-(CH_3NH)phenyl
126. 2-pyrimidyl 3-(($CH_3)_2NCH_2$)-4-pyridyl
127. 2-pyrimidyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
128. 2-pyrimidyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
129. 2-pyrimidyl 2-(($CH_3)_2NCH_2$)phenyl
130. 2-pyrimidyl 2-((CH_3)$NHCH_2$)phenyl
131. 2-pyrimidyl 2-((CH_3CH_2)$NHCH_2$)phenyl
132. 2-pyrimidyl 2-(($CH_3CH_2)_2NCH_2$)phenyl
133. 2-pyrimidyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
134. 2-pyrimidyl 2-((($CH_3)_2CH$)$NHCH_2$)phenyl
135. 2-pyrimidyl 2-((($CH_3)_2CH)_2NCH_2$)phenyl
136. 2-pyrimidyl 2-((cyclopropyl)$NHCH_2$)phenyl
137. 2-pyrimidyl 2-((cyclopropyl)$_2NCH_2$)phenyl
138. 2-pyrimidyl 2-((cyclobutyl)$NHCH_2$)phenyl
139. 2-pyrimidyl 2-((cyclobutyl)$_2NCH_2$)phenyl
140. 2-pyrimidyl 2-((cyclopentyl)$NHCH_2$)phenyl
141. 2-pyrimidyl 2-((cyclopentyl)$_2NCH_2$)phenyl
142. 2-pyrimidyl 2-((cyclohexyl)$NHCH_2$)phenyl
143. 2-pyrimidyl 2-((cyclohexyl)$_2NCH_2$)phenyl
144. 2-pyrimidyl 1-CH_3-2-imidazolyl
145. 2-pyrimidyl 2-CH_3-1-imidazolyl
146. 2-pyrimidyl 2-(($CH_3)_2NCH_2$)-1-imidazolyl
147. 2-pyrimidyl 2-((CH_3)$NHCH_2$)-1-imidazolyl
148. 2-pyrimidyl 2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
149. 2-pyrimidyl 2-(($CH_3CH_2)_2NCH_2$)-1-imidazolyl
150. 2-pyrimidyl 2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
151. 2-pyrimidyl 2-((($CH_3)_2CH$)$NHCH_2$)-1-imidazolyl
152. 2-pyrimidyl 2-((($CH_3)_2CH)_2NCH_2$)-1-imidazolyl
153. 2-pyrimidyl 2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
154. 2-pyrimidyl 2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
155. 2-pyrimidyl 2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
156. 2-pyrimidyl 2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
157. 2-pyrimidyl 2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
158. 2-pyrimidyl 2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
159. 2-pyrimidyl 2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
160. 2-pyrimidyl 2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
161. 5-pyrimidyl 2-(NH_2SO_2)phenyl
162. 5-pyrimidyl 2-(CH_3SO_2)phenyl
163. 5-pyrimidyl 3-NH_2SO_2-4-pyridyl
164. 5-pyrimidyl 3-CH_3SO_2-4-pyridyl
165. 5-pyrimidyl 2-(CH_3NH)phenyl
166. 5-pyrimidyl 3-(($CH_3)_2NCH_2$)-4-pyridyl
167. 5-pyrimidyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
168. 5-pyrimidyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
169. 5-pyrimidyl 2-(($CH_3)_2NCH_2$)phenyl
170. 5-pyrimidyl 2-((CH_3)$NHCH_2$)phenyl
171. 5-pyrimidyl 2-((CH_3CH_2)$NHCH_2$)phenyl
172. 5-pyrimidyl 2-(($CH_3CH_2)_2NCH_2$)phenyl
173. 5-pyrimidyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
174. 5-pyrimidyl 2-((($CH_3)_2CH$)$NHCH_2$)phenyl
175. 5-pyrimidyl 2-((($CH_3)_2CH)_2NCH_2$)phenyl
176. 5-pyrimidyl 2-((cyclopropyl)$NHCH_2$)phenyl

177. 5-pyrimidyl 2-((cyclopropyl)$_2$NCH$_2$)phenyl
178. 5-pyrimidyl 2-((cyclobutyl)NHCH$_2$)phenyl
179. 5-pyrimidyl 2-((cyclobutyl)$_2$NCH$_2$)phenyl
180. 5-pyrimidyl 2-((cyclopentyl)NHCH$_2$)phenyl
181. 5-pyrimidyl 2-((cyclopentyl)$_2$NCH$_2$)phenyl
182. 5-pyrimidyl 2-((cyclohexyl)NHCH$_2$)phenyl
183. 5-pyrimidyl 2-((cyclohexyl)$_2$NCH$_2$)phenyl
184. 5-pyrimidyl 1-CH$_3$-2-imidazolyl
185. 5-pyrimidyl 2-CH$_3$-1-imidazolyl
186. 5-pyrimidyl 2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
187. 5-pyrimidyl 2-((CH$_3$)NHCH$_2$)-1-imidazolyl
188. 5-pyrimidyl 2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
189. 5-pyrimidyl 2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
190. 5-pyrimidyl 2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
191. 5-pyrimidyl 2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
192. 5-pyrimidyl 2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
193. 5-pyrimidyl 2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
194. 5-pyrimidyl 2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
195. 5-pyrimidyl 2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
196. 5-pyrimidyl 2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
197. 5-pyrimidyl 2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
198. 5-pyrimidyl 2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
199. 5-pyrimidyl 2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
200. 5-pyrimidyl 2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
201. 2-Cl-phenyl 2-(NH$_2$SO$_2$)phenyl
202. 2-Cl-phenyl 2-(CH$_3$SO$_2$)phenyl
203. 2-Cl-phenyl 3-NH$_2$SO$_2$-4-pyridyl
204. 2-Cl-phenyl 3-CH$_3$SO$_2$-4-pyridyl
205. 2-Cl-phenyl 2-(CH$_3$NH)phenyl
206. 2-Cl-phenyl 3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
207. 2-Cl-phenyl 2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
208. 2-Cl-phenyl 2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
209. 2-Cl-phenyl 2-((CH$_3$)$_2$NCH$_2$)phenyl
210. 2-Cl-phenyl 2-((CH$_3$)NHCH$_2$)phenyl
211. 2-Cl-phenyl 2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
212. 2-Cl-phenyl 2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
213. 2-Cl-phenyl 2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
214. 2-Cl-phenyl 2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
215. 2-Cl-phenyl 2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
216. 2-Cl-phenyl 2-((cyclopropyl)NHCH$_2$)phenyl
217. 2-Cl-phenyl 2-((cyclopropyl)$_2$NCH$_2$)phenyl
218. 2-Cl-phenyl 2-((cyclobutyl)NHCH$_2$)phenyl
219. 2-Cl-phenyl 2-((cyclobutyl)$_2$NCH$_2$)phenyl
220. 2-Cl-phenyl 2-((cyclopentyl)NHCH$_2$)phenyl
221. 2-Cl-phenyl 2-((cyclopentyl)$_2$NCH$_2$)phenyl
222. 2-Cl-phenyl 2-((cyclohexyl)NHCH$_2$)phenyl
223. 2-Cl-phenyl 2-((cyclohexyl)$_2$NCH$_2$)phenyl
224. 2-Cl-phenyl 1-CH$_3$-2-imidazolyl
225. 2-Cl-phenyl 2-CH$_3$-1-imidazolyl
226. 2-Cl-phenyl 2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
227. 2-Cl-phenyl 2-((CH$_3$)NHCH$_2$)-1-imidazolyl
228. 2-Cl-phenyl 2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
229. 2-Cl-phenyl 2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl

230. 2-Cl-phenyl 2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
231. 2-Cl-phenyl 2-((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
232. 2-Cl-phenyl 2-((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
233. 2-Cl-phenyl 2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
234. 2-Cl-phenyl 2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
235. 2-Cl-phenyl 2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
236. 2-Cl-phenyl 2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
237. 2-Cl-phenyl 2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
238. 2-Cl-phenyl 2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
239. 2-Cl-phenyl 2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
240. 2-Cl-phenyl 2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
241. 2-F-phenyl 2-(NH$_2$SO$_2$)phenyl
242. 2-F-phenyl 2-(CH$_3$SO$_2$)phenyl
243. 2-F-phenyl 3-NH$_2$SO$_2$-4-pyridyl
244. 2-F-phenyl 3-CH$_3$SO$_2$-4-pyridyl
245. 2-F-phenyl 2-(CH$_3$NH)phenyl
246. 2-F-phenyl 3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
247. 2-F-phenyl 2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
248. 2-F-phenyl 2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
249. 2-F-phenyl 2-((CH$_3$)$_2$NCH$_2$)phenyl
250. 2-F-phenyl 2-((CH$_3$)NHCH$_2$)phenyl
251. 2-F-phenyl 2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
252. 2-F-phenyl 2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
253. 2-F-phenyl 2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
254. 2-F-phenyl 2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
255. 2-F-phenyl 2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
256. 2-F-phenyl 2-((cyclopropyl)NHCH$_2$)phenyl
257. 2-F-phenyl 2-((cyclopropyl)$_2$NCH$_2$)phenyl
258. 2-F-phenyl 2-((cyclobutyl)NHCH$_2$)phenyl
259. 2-F-phenyl 2-((cyclobutyl)$_2$NCH$_2$)phenyl
260. 2-F-phenyl 2-((cyclopentyl)NHCH$_2$)phenyl
261. 2-F-phenyl 2-((cyclopentyl)$_2$NCH$_2$)phenyl
262. 2-F-phenyl 2-((cyclohexyl)NHCH$_2$)phenyl
263. 2-F-phenyl 2-((cyclohexyl)$_2$NCH$_2$)phenyl
264. 2-F-phenyl 1-CH$_3$-2-imidazolyl
265. 2-F-phenyl 2-CH$_3$-1-imidazolyl
266. 2-F-phenyl 2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
267. 2-F-phenyl 2-((CH$_3$)NHCH$_2$)-1-imidazolyl
268. 2-F-phenyl 2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
269. 2-F-phenyl 2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
270. 2-F-phenyl 2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
271. 2-F-phenyl 2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
272. 2-F-phenyl 2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
273. 2-F-phenyl 2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
274. 2-F-phenyl 2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
275. 2-F-phenyl 2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
276. 2-F-phenyl 2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
277. 2-F-phenyl 2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
278. 2-F-phenyl 2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
279. 2-F-phenyl 2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
280. 2-F-phenyl 2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
281. 2,6-diF-phenyl 2-(NH$_2$SO$_2$)phenyl
282. 2,6-diF-phenyl 2-(CH$_3$SO$_2$)phenyl

283. 2,6-diF-phenyl 3-NH_2SO_2-4-pyridyl
284. 2,6-diF-phenyl 3-CH_3SO_2-4-pyridyl
285. 2,6-diF-phenyl 2-(CH_3NH)phenyl
286. 2,6-diF-phenyl 3-((CH_3)$_2NCH_2$)-4-pyridyl
287. 2,6-diF-phenyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
288. 2,6-diF-phenyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
289. 2,6-diF-phenyl 2-((CH_3)$_2NCH_2$)phenyl
290. 2,6-diF-phenyl 2-((CH_3)$NHCH_2$)phenyl
291. 2,6-diF-phenyl 2-((CH_3CH_2)$NHCH_2$)phenyl
292. 2,6-diF-phenyl 2-((CH_3CH_2)$_2NCH_2$)phenyl
293. 2,6-diF-phenyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
294. 2,6-diF-phenyl 2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
295. 2,6-diF-phenyl 2-(((CH_3)$_2$CH)$_2NCH_2$)phenyl
296. 2,6-diF-phenyl 2-((cyclopropyl)$NHCH_2$)phenyl
297. 2,6-diF-phenyl 2-((cyclopropyl)$_2NCH_2$)phenyl
298. 2,6-diF-phenyl 2-((cyclobutyl)$NHCH_2$)phenyl
299. 2,6-diF-phenyl 2-((cyclobutyl)$_2NCH_2$)phenyl
300. 2,6-diF-phenyl 2-((cyclopentyl)$NHCH_2$)phenyl
301. 2,6-diF-phenyl 2-((cyclopentyl)$_2NCH_2$)phenyl
302. 2,6-diF-phenyl 2-((cyclohexyl)$NHCH_2$)phenyl
303. 2,6-diF-phenyl 2-((cyclohexyl)$_2NCH_2$)phenyl
304. 2,6-diF-phenyl 1-CH_3-2-imidazolyl
305. 2,6-diF-phenyl 2-CH_3-1-imidazolyl
306. 2,6-diF-phenyl 2-((CH_3)$_2NCH_2$)-1-imidazolyl
307. 2,6-diF-phenyl 2-((CH_3)$NHCH_2$)-1-imidazolyl
308. 2,6-diF-phenyl 2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
309. 2,6-diF-phenyl 2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
310. 2,6-diF-phenyl 2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
311. 2,6-diF-phenyl 2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
312. 2,6-diF-phenyl 2-(((CH_3)$_2$CH)$_2NCH_2$)-1-imidazolyl
313. 2,6-diF-phenyl 2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
314. 2,6-diF-phenyl 2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
315. 2,6-diF-phenyl 2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
316. 2,6-diF-phenyl 2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
317. 2,6-diF-phenyl 2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
318. 2,6-diF-phenyl 2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
319. 2,6-diF-phenyl 2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
320. 2,6-diF-phenyl 2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
321. piperidinyl 2-(NH_2SO_2)phenyl
322. piperidinyl 2-(CH_3SO_2)phenyl
323. piperidinyl 3-NH_2SO_2-4-pyridyl
324. piperidinyl 3-CH_3SO_2-4-pyridyl
325. piperidinyl 2-(CH_3NH)phenyl
326. piperidinyl 3-((CH_3)$_2NCH_2$)-4-pyridyl
327. piperidinyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
328. piperidinyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
329. piperidinyl 2-((CH_3)$_2NCH_2$)phenyl
330. piperidinyl 2-((CH_3)$NHCH_2$)phenyl
331. piperidinyl 2-((CH_3CH_2)$NHCH_2$)phenyl
332. piperidinyl 2-((CH_3CH_2)$_2NCH_2$)phenyl
333. piperidinyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
334. piperidinyl 2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
335. piperidinyl 2-(((CH_3)$_2$CH)$_2NCH_2$)phenyl

336. piperidinyl 2-((cyclopropyl)$NHCH_2$)phenyl
337. piperidinyl 2-((cyclopropyl)$_2NCH_2$)phenyl
338. piperidinyl 2-((cyclobutyl)$NHCH_2$)phenyl
339. piperidinyl 2-((cyclobutyl)$_2NCH_2$)phenyl
340. piperidinyl 2-((cyclopentyl)$NHCH_2$)phenyl
341. piperidinyl 2-((cyclopentyl)$_2NCH_2$)phenyl
342. piperidinyl 2-((cyclohexyl)$NHCH_2$)phenyl
343. piperidinyl 2-((cyclohexyl)$_2NCH_2$)phenyl
344. piperidinyl 1-CH_3-2-imidazolyl
345. piperidinyl 2-CH_3-1-imidazolyl
346. piperidinyl 2-((CH_3)$_2NCH_2$)-1-imidazolyl
347. piperidinyl 2-((CH_3)$NHCH_2$)-1-imidazolyl
348. piperidinyl 2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
349. piperidinyl 2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
350. piperidinyl 2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
351. piperidinyl 2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
352. piperidinyl 2-(((CH_3)$_2$CH)$_2NCH_2$)-1-imidazolyl
353. piperidinyl 2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
354. piperidinyl 2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
355. piperidinyl 2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
356. piperidinyl 2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
357. piperidinyl 2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
358. piperidinyl 2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
359. piperidinyl 2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
360. piperidinyl 2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl

Table 2

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is CH_2CH_3.

Table 3

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is CF_3.

Table 4

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is SCH_3.

Table 5

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is $SOCH_3$.

Table 6

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is SO_2CH_3.

Table 7

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is Cl.

Table 8

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is F.

Table 9

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is CO_2CH_3.

Table 10

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is CH_2OCH_3.

Table 11

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is $CONH_2$.

Table 12

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is CN.

Table 13

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is CH_2NH_2.

Table 14

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

R^{1a} is $CH_2NHSO_2CH_3$.

Table 15

Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

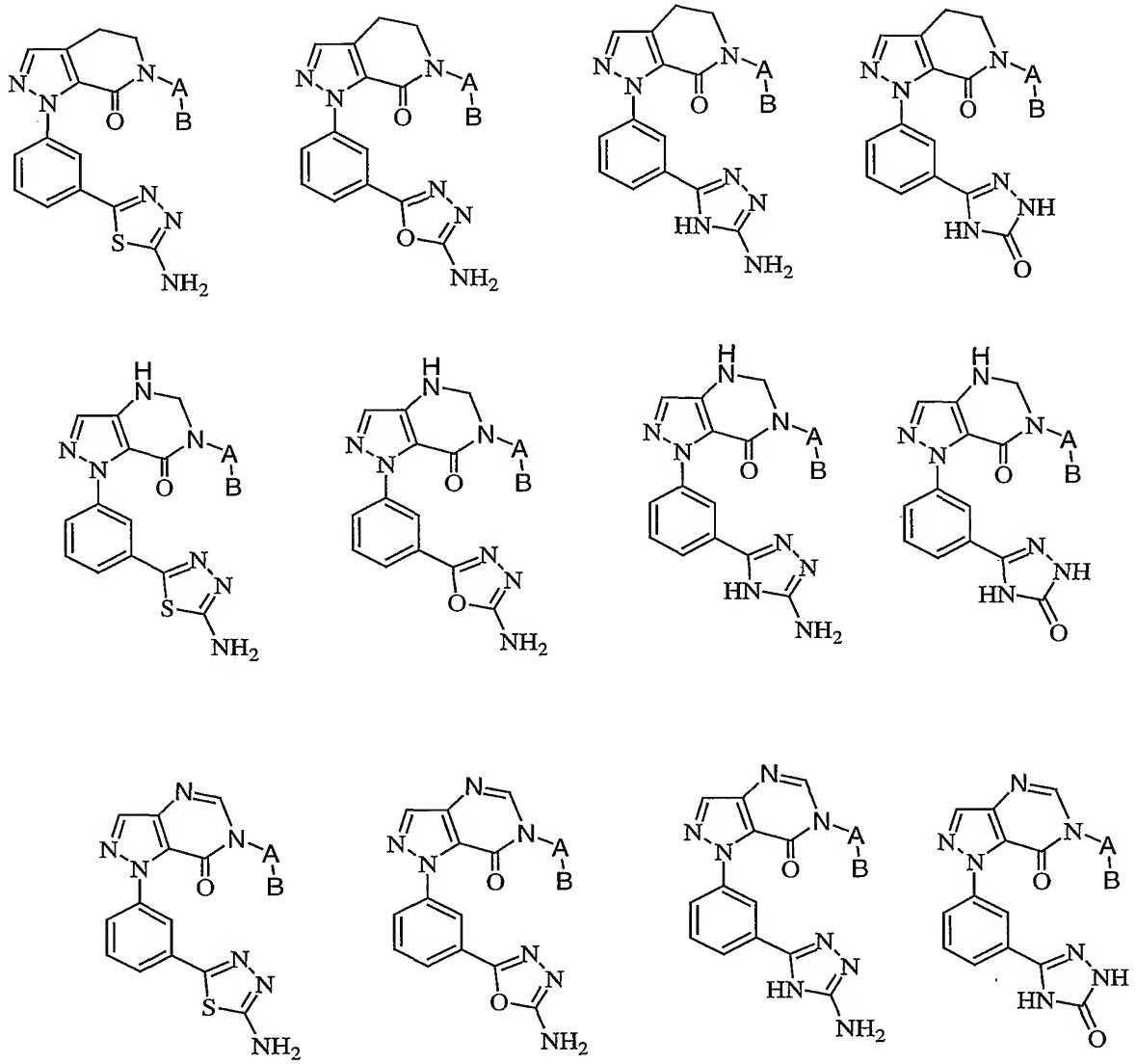
R^{1a} is 1-imidazolyl-CH_2.

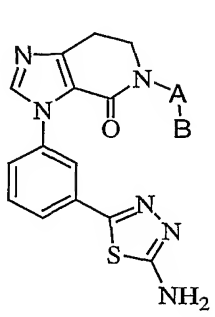
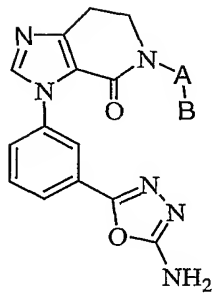
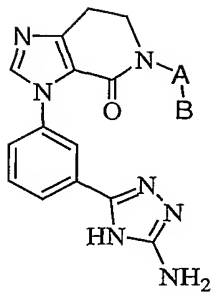
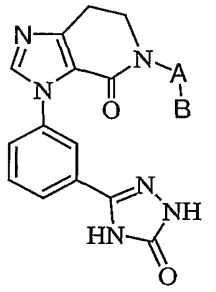
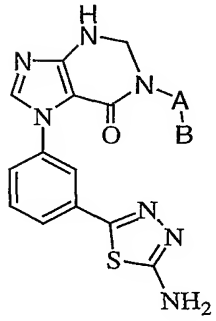
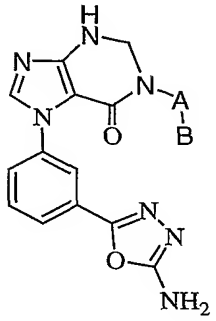
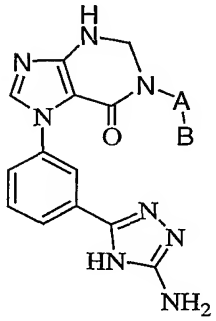
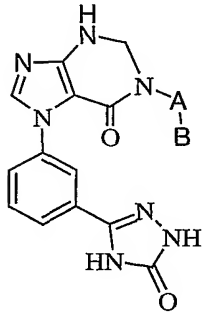
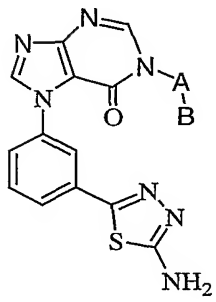
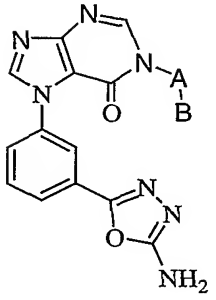
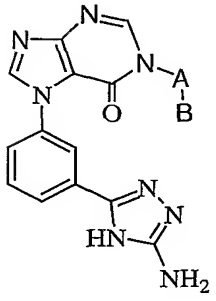
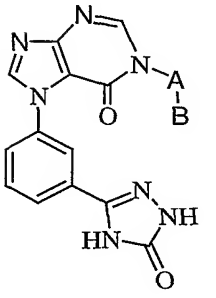
Table 16

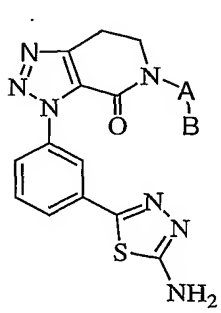
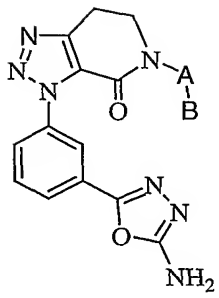
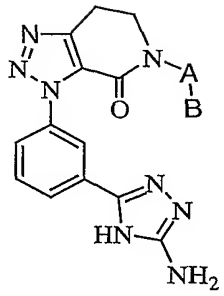
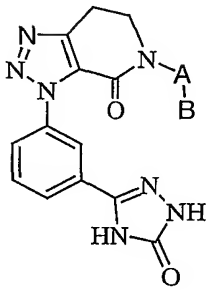
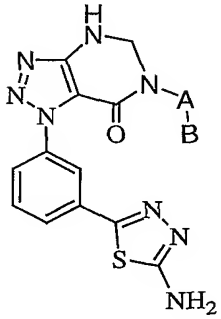
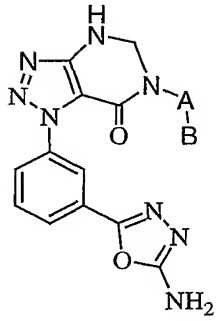
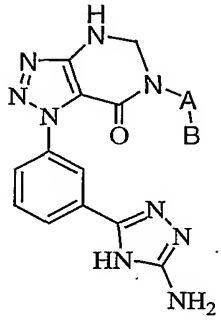
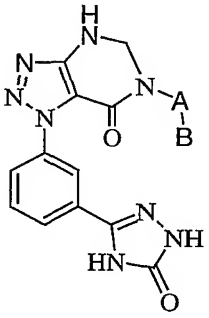
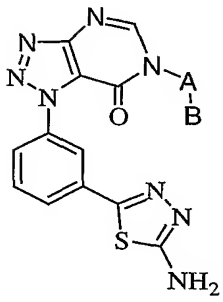
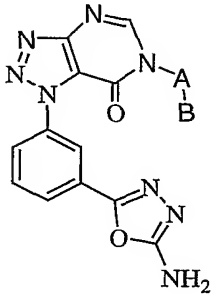
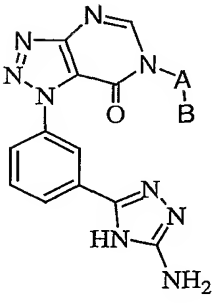
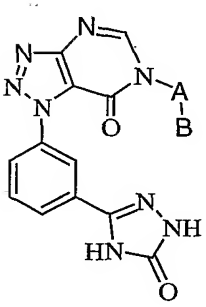
Examples 1-360 use the structures from Table 1 and the corresponding A and B groups from Examples 1-360 of Table 1, and:

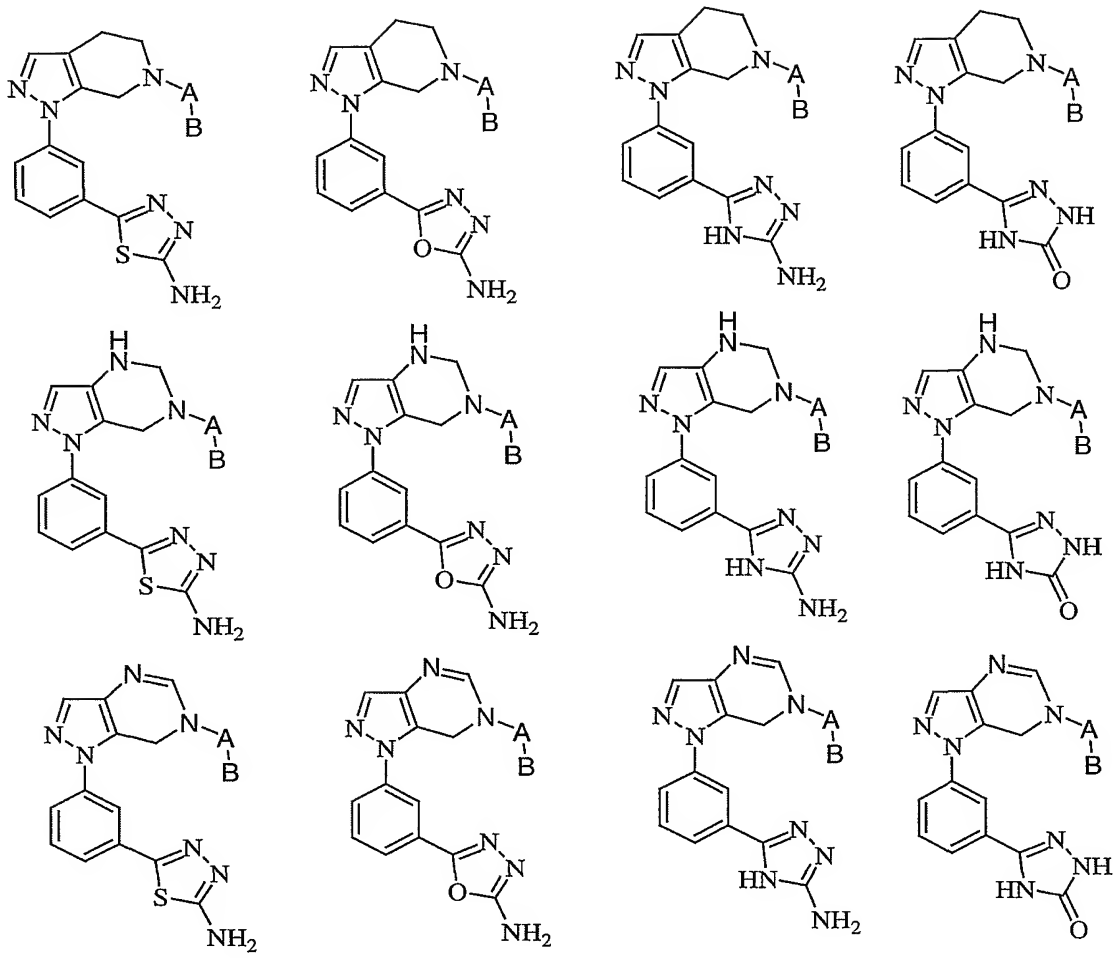
R^{1a} is 1-tetrazolyl-CH_2-.

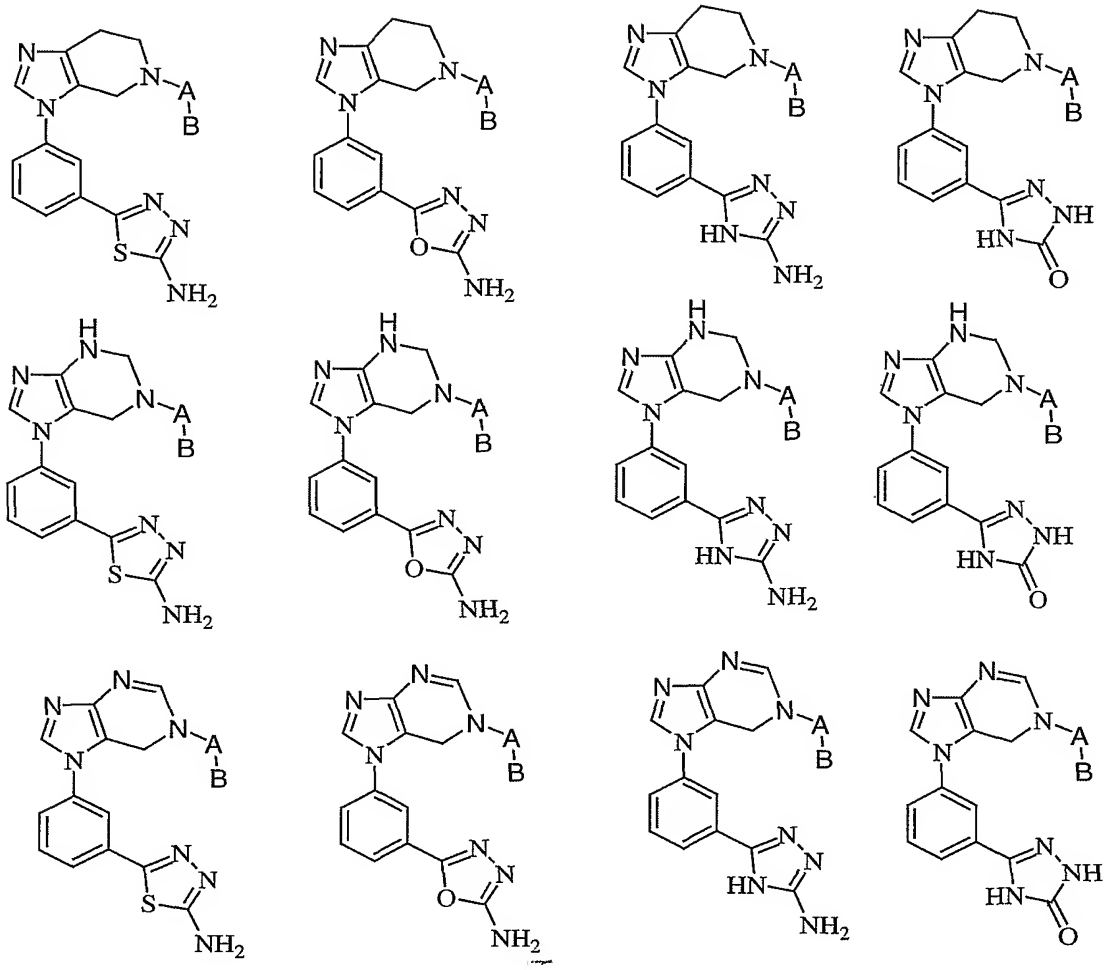
Table 17

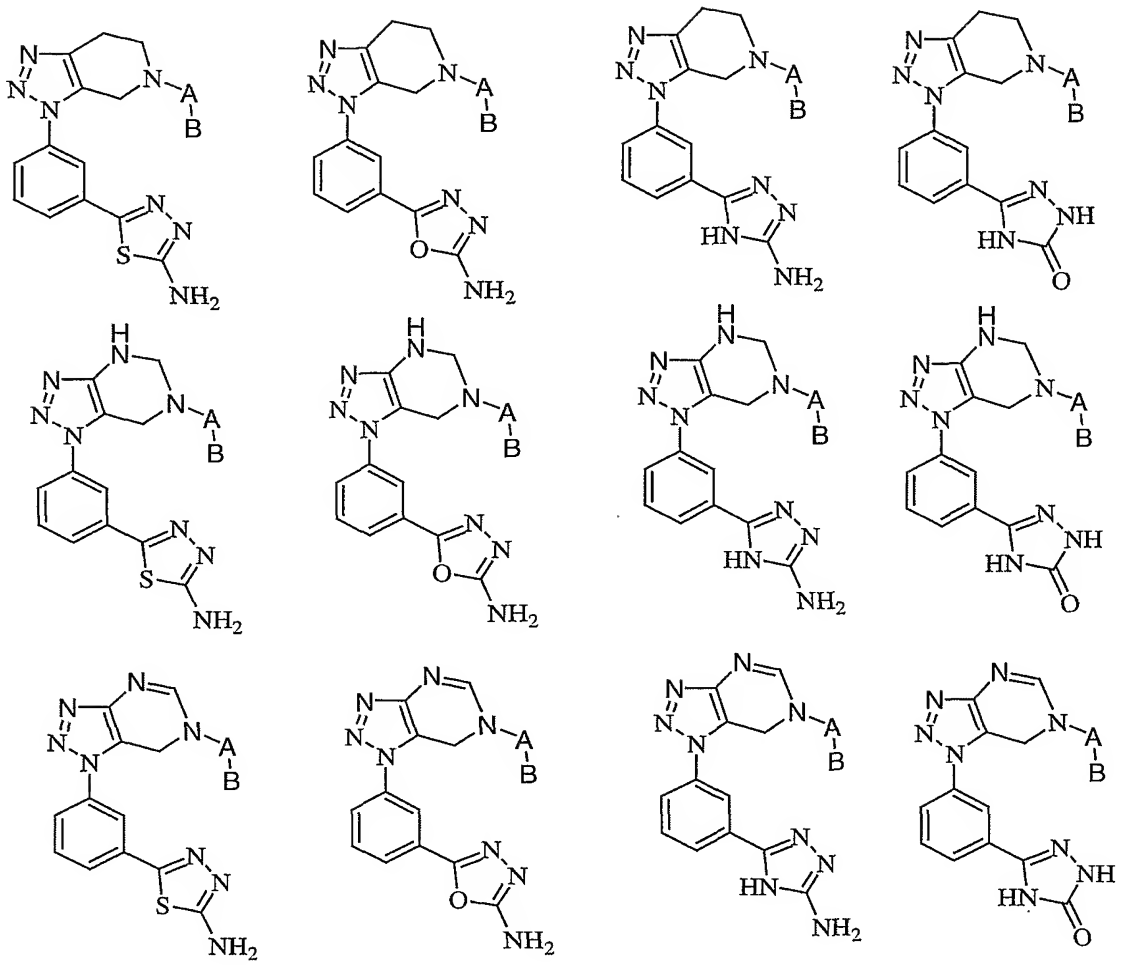








Ex#	A	B
1.	phenyl	2-(NH_2SO_2)phenyl
2.	phenyl	2-(CH_3SO_2)phenyl
3.	phenyl	3-NH_2SO_2-4-pyridyl
4.	phenyl	3-CH_3SO_2-4-pyridyl
5.	phenyl	2-(CH_3NH)phenyl
6.	phenyl	3-(($(CH_3)_2NCH_2$)-4-pyridyl
7.	phenyl	2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
8.	phenyl	2-(N-(4-HO-piperidinyl)CH_2)phenyl
9.	phenyl	2-(($(CH_3)_2NCH_2$)phenyl
10.	phenyl	2-((CH_3)$NHCH_2$)phenyl
11.	phenyl	2-((CH_3CH_2)$NHCH_2$)phenyl
12.	phenyl	2-(($CH_3CH_2)_2NCH_2$)phenyl
13.	phenyl	2-((CH_3CH_2)N(CH_3)CH_2)phenyl
14.	phenyl	2-((($(CH_3)_2CH$)$NHCH_2$)phenyl
15.	phenyl	2-((($(CH_3)_2CH)_2NCH_2$)phenyl
16.	phenyl	2-((cyclopropyl)$NHCH_2$)phenyl
17.	phenyl	2-((cyclopropyl)$_2NCH_2$)phenyl
18.	phenyl	2-((cyclobutyl)$NHCH_2$)phenyl
19.	phenyl	2-((cyclobutyl)$_2NCH_2$)phenyl
20.	phenyl	2-((cyclopentyl)$NHCH_2$)phenyl

	21.	phenyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
	22.	phenyl	2-((cyclohexyl)NHCH$_2$)phenyl
	23.	phenyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
	24.	phenyl	1-CH$_3$-2-imidazolyl
5	25.	phenyl	2-CH$_3$-1-imidazolyl
	26.	phenyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
	27.	phenyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
	28.	phenyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
	29.	phenyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
10	30.	phenyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
	31.	phenyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
	32.	phenyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
	33.	phenyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
	34.	phenyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
15	35.	phenyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
	36.	phenyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
	37.	phenyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
	38.	phenyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
	39.	phenyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
20	40.	phenyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
	41.	2-pyridyl	2-(NH$_2$SO$_2$)phenyl
	42.	2-pyridyl	2-(CH$_3$SO$_2$)phenyl
	43.	2-pyridyl	3-NH$_2$SO$_2$-4-pyridyl
	44.	2-pyridyl	3-CH$_3$SO$_2$-4-pyridyl
25	45.	2-pyridyl	2-(CH$_3$NH)phenyl
	46.	2-pyridyl	3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
	47.	2-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
	48.	2-pyridyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
	49.	2-pyridyl	2-((CH$_3$)$_2$NCH$_2$)phenyl
30	50.	2-pyridyl	2-((CH$_3$)NHCH$_2$)phenyl
	51.	2-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
	52.	2-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
	53.	2-pyridyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
	54.	2-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
35	55.	2-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
	56.	2-pyridyl	2-((cyclopropyl)NHCH$_2$)phenyl
	57.	2-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
	58.	2-pyridyl	2-((cyclobutyl)NHCH$_2$)phenyl
	59.	2-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
40	60.	2-pyridyl	2-((cyclopentyl)NHCH$_2$)phenyl
	61.	2-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
	62.	2-pyridyl	2-((cyclohexyl)NHCH$_2$)phenyl
	63.	2-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
	64.	2-pyridyl	1-CH$_3$-2-imidazolyl
45	65.	2-pyridyl	2-CH$_3$-1-imidazolyl
	66.	2-pyridyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
	67.	2-pyridyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
	68.	2-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
	69.	2-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
50	70.	2-pyridyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
	71.	2-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
	72.	2-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
	73.	2-pyridyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl

74.	2-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
75.	2-pyridyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
76.	2-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
77.	2-pyridyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
78.	2-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
79.	2-pyridyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
80.	2-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
81.	3-pyridyl	2-(NH$_2$SO$_2$)phenyl
82.	3-pyridyl	2-(CH$_3$SO$_2$)phenyl
83.	3-pyridyl	3-NH$_2$SO$_2$-4-pyridyl
84.	3-pyridyl	3-CH$_3$SO$_2$-4-pyridyl
85.	3-pyridyl	2-(CH$_3$NH)phenyl
86.	3-pyridyl	3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl
87.	3-pyridyl	2-(N-(3-R-HO-pyrrolidinyl)CH$_2$)phenyl
88.	3-pyridyl	2-(N-(4-HO-piperidinyl)CH$_2$)phenyl
89.	3-pyridyl	2-((CH$_3$)$_2$NCH$_2$)phenyl
90.	3-pyridyl	2-((CH$_3$)NHCH$_2$)phenyl
91.	3-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)phenyl
92.	3-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)phenyl
93.	3-pyridyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)phenyl
94.	3-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)phenyl
95.	3-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)phenyl
96.	3-pyridyl	2-((cyclopropyl)NHCH$_2$)phenyl
97.	3-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)phenyl
98.	3-pyridyl	2-((cyclobutyl)NHCH$_2$)phenyl
99.	3-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)phenyl
100.	3-pyridyl	2-((cyclopentyl)NHCH$_2$)phenyl
101.	3-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)phenyl
102.	3-pyridyl	2-((cyclohexyl)NHCH$_2$)phenyl
103.	3-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)phenyl
104.	3-pyridyl	1-CH$_3$-2-imidazolyl
105.	3-pyridyl	2-CH$_3$-1-imidazolyl
106.	3-pyridyl	2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
107.	3-pyridyl	2-((CH$_3$)NHCH$_2$)-1-imidazolyl
108.	3-pyridyl	2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
109.	3-pyridyl	2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
110.	3-pyridyl	2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
111.	3-pyridyl	2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
112.	3-pyridyl	2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
113.	3-pyridyl	2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
114.	3-pyridyl	2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
115.	3-pyridyl	2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
116.	3-pyridyl	2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
117.	3-pyridyl	2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
118.	3-pyridyl	2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
119.	3-pyridyl	2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
120.	3-pyridyl	2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl
121.	2-pyrimidyl	2-(NH$_2$SO$_2$)phenyl
122.	2-pyrimidyl	2-(CH$_3$SO$_2$)phenyl
123.	2-pyrimidyl	3-NH$_2$SO$_2$-4-pyridyl
124.	2-pyrimidyl	3-CH$_3$SO$_2$-4-pyridyl
125.	2-pyrimidyl	2-(CH$_3$NH)phenyl
126.	2-pyrimidyl	3-((CH$_3$)$_2$NCH$_2$)-4-pyridyl

127. 2-pyrimidyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
128. 2-pyrimidyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
129. 2-pyrimidyl 2-((CH_3)$_2$$NCH_2$)phenyl
130. 2-pyrimidyl 2-((CH_3)$NHCH_2$)phenyl
131. 2-pyrimidyl 2-((CH_3CH_2)$NHCH_2$)phenyl
132. 2-pyrimidyl 2-((CH_3CH_2)$_2$$NCH_2$)phenyl
133. 2-pyrimidyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
134. 2-pyrimidyl 2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
135. 2-pyrimidyl 2-(((CH_3)$_2$CH)$_2$$NCH_2$)phenyl
136. 2-pyrimidyl 2-((cyclopropyl)$NHCH_2$)phenyl
137. 2-pyrimidyl 2-((cyclopropyl)$_2$$NCH_2$)phenyl
138. 2-pyrimidyl 2-((cyclobutyl)$NHCH_2$)phenyl
139. 2-pyrimidyl 2-((cyclobutyl)$_2$$NCH_2$)phenyl
140. 2-pyrimidyl 2-((cyclopentyl)$NHCH_2$)phenyl
141. 2-pyrimidyl 2-((cyclopentyl)$_2$$NCH_2$)phenyl
142. 2-pyrimidyl 2-((cyclohexyl)$NHCH_2$)phenyl
143. 2-pyrimidyl 2-((cyclohexyl)$_2$$NCH_2$)phenyl
144. 2-pyrimidyl 1-CH_3-2-imidazolyl
145. 2-pyrimidyl 2-CH_3-1-imidazolyl
146. 2-pyrimidyl 2-((CH_3)$_2$$NCH_2$)-1-imidazolyl
147. 2-pyrimidyl 2-((CH_3)$NHCH_2$)-1-imidazolyl
148. 2-pyrimidyl 2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
149. 2-pyrimidyl 2-((CH_3CH_2)$_2$$NCH_2$)-1-imidazolyl
150. 2-pyrimidyl 2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
151. 2-pyrimidyl 2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
152. 2-pyrimidyl 2-(((CH_3)$_2$CH)$_2$$NCH_2$)-1-imidazolyl
153. 2-pyrimidyl 2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
154. 2-pyrimidyl 2-((cyclopropyl)$_2$$NCH_2$)-1-imidazolyl
155. 2-pyrimidyl 2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
156. 2-pyrimidyl 2-((cyclobutyl)$_2$$NCH_2$)-1-imidazolyl
157. 2-pyrimidyl 2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
158. 2-pyrimidyl 2-((cyclopentyl)$_2$$NCH_2$)-1-imidazolyl
159. 2-pyrimidyl 2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
160. 2-pyrimidyl 2-((cyclohexyl)$_2$$NCH_2$)-1-imidazolyl
161. 5-pyrimidyl 2-(NH_2SO_2)phenyl
162. 5-pyrimidyl 2-(CH_3SO_2)phenyl
163. 5-pyrimidyl 3-NH_2SO_2-4-pyridyl
164. 5-pyrimidyl 3-CH_3SO_2-4-pyridyl
165. 5-pyrimidyl 2-(CH_3NH)phenyl
166. 5-pyrimidyl 3-((CH_3)$_2$$NCH_2$)-4-pyridyl
167. 5-pyrimidyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
168. 5-pyrimidyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
169. 5-pyrimidyl 2-((CH_3)$_2$$NCH_2$)phenyl
170. 5-pyrimidyl 2-((CH_3)$NHCH_2$)phenyl
171. 5-pyrimidyl 2-((CH_3CH_2)$NHCH_2$)phenyl
172. 5-pyrimidyl 2-((CH_3CH_2)$_2$$NCH_2$)phenyl
173. 5-pyrimidyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
174. 5-pyrimidyl 2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
175. 5-pyrimidyl 2-(((CH_3)$_2$CH)$_2$$NCH_2$)phenyl
176. 5-pyrimidyl 2-((cyclopropyl)$NHCH_2$)phenyl
177. 5-pyrimidyl 2-((cyclopropyl)$_2$$NCH_2$)phenyl
178. 5-pyrimidyl 2-((cyclobutyl)$NHCH_2$)phenyl
179. 5-pyrimidyl 2-((cyclobutyl)$_2$$NCH_2$)phenyl

180. 5-pyrimidyl 2-((cyclopentyl)$NHCH_2$)phenyl
181. 5-pyrimidyl 2-((cyclopentyl)$_2NCH_2$)phenyl
182. 5-pyrimidyl 2-((cyclohexyl)$NHCH_2$)phenyl
183. 5-pyrimidyl 2-((cyclohexyl)$_2NCH_2$)phenyl
184. 5-pyrimidyl 1-CH_3-2-imidazolyl
185. 5-pyrimidyl 2-CH_3-1-imidazolyl
186. 5-pyrimidyl 2-((CH_3)$_2NCH_2$)-1-imidazolyl
187. 5-pyrimidyl 2-((CH_3)$NHCH_2$)-1-imidazolyl
188. 5-pyrimidyl 2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
189. 5-pyrimidyl 2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
190. 5-pyrimidyl 2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
191. 5-pyrimidyl 2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
192. 5-pyrimidyl 2-(((CH_3)$_2$CH)$_2NCH_2$)-1-imidazolyl
193. 5-pyrimidyl 2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
194. 5-pyrimidyl 2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
195. 5-pyrimidyl 2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
196. 5-pyrimidyl 2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
197. 5-pyrimidyl 2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
198. 5-pyrimidyl 2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
199. 5-pyrimidyl 2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
200. 5-pyrimidyl 2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
201. 2-Cl-phenyl 2-(NH_2SO_2)phenyl
202. 2-Cl-phenyl 2-(CH_3SO_2)phenyl
203. 2-Cl-phenyl 3-NH_2SO_2-4-pyridyl
204. 2-Cl-phenyl 3-CH_3SO_2-4-pyridyl
205. 2-Cl-phenyl 2-(CH_3NH)phenyl
206. 2-Cl-phenyl 3-((CH_3)$_2NCH_2$)-4-pyridyl
207. 2-Cl-phenyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
208. 2-Cl-phenyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
209. 2-Cl-phenyl 2-((CH_3)$_2NCH_2$)phenyl
210. 2-Cl-phenyl 2-((CH_3)$NHCH_2$)phenyl
211. 2-Cl-phenyl 2-((CH_3CH_2)$NHCH_2$)phenyl
212. 2-Cl-phenyl 2-((CH_3CH_2)$_2NCH_2$)phenyl
213. 2-Cl-phenyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
214. 2-Cl-phenyl 2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
215. 2-Cl-phenyl 2-(((CH_3)$_2$CH)$_2NCH_2$)phenyl
216. 2-Cl-phenyl 2-((cyclopropyl)$NHCH_2$)phenyl
217. 2-Cl-phenyl 2-((cyclopropyl)$_2NCH_2$)phenyl
218. 2-Cl-phenyl 2-((cyclobutyl)$NHCH_2$)phenyl
219. 2-Cl-phenyl 2-((cyclobutyl)$_2NCH_2$)phenyl
220. 2-Cl-phenyl 2-((cyclopentyl)$NHCH_2$)phenyl
221. 2-Cl-phenyl 2-((cyclopentyl)$_2NCH_2$)phenyl
222. 2-Cl-phenyl 2-((cyclohexyl)$NHCH_2$)phenyl
223. 2-Cl-phenyl 2-((cyclohexyl)$_2NCH_2$)phenyl
224. 2-Cl-phenyl 1-CH_3-2-imidazolyl
225. 2-Cl-phenyl 2-CH_3-1-imidazolyl
226. 2-Cl-phenyl 2-((CH_3)$_2NCH_2$)-1-imidazolyl
227. 2-Cl-phenyl 2-((CH_3)$NHCH_2$)-1-imidazolyl
228. 2-Cl-phenyl 2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
229. 2-Cl-phenyl 2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
230. 2-Cl-phenyl 2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
231. 2-Cl-phenyl 2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
232. 2-Cl-phenyl 2-(((CH_3)$_2$CH)$_2NCH_2$)-1-imidazolyl

233. 2-Cl-phenyl 2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
234. 2-Cl-phenyl 2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
235. 2-Cl-phenyl 2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
236. 2-Cl-phenyl 2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
237. 2-Cl-phenyl 2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
238. 2-Cl-phenyl 2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
239. 2-Cl-phenyl 2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
240. 2-Cl-phenyl 2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
241. 2-F-phenyl 2-(NH_2SO_2)phenyl
242. 2-F-phenyl 2-(CH_3SO_2)phenyl
243. 2-F-phenyl 3-NH_2SO_2-4-pyridyl
244. 2-F-phenyl 3-CH_3SO_2-4-pyridyl
245. 2-F-phenyl 2-(CH_3NH)phenyl
246. 2-F-phenyl 3-((CH_3)$_2NCH_2$)-4-pyridyl
247. 2-F-phenyl 2-(N-(3-R-HO-pyrrolidinyl)CH_2)phenyl
248. 2-F-phenyl 2-(N-(4-HO-piperidinyl)CH_2)phenyl
249. 2-F-phenyl 2-((CH_3)$_2NCH_2$)phenyl
250. 2-F-phenyl 2-((CH_3)$NHCH_2$)phenyl
251. 2-F-phenyl 2-((CH_3CH_2)$NHCH_2$)phenyl
252. 2-F-phenyl 2-((CH_3CH_2)$_2NCH_2$)phenyl
253. 2-F-phenyl 2-((CH_3CH_2)N(CH_3)CH_2)phenyl
254. 2-F-phenyl 2-(((CH_3)$_2$CH)$NHCH_2$)phenyl
255. 2-F-phenyl 2-(((CH_3)$_2$CH)$_2NCH_2$)phenyl
256. 2-F-phenyl 2-((cyclopropyl)$NHCH_2$)phenyl
257. 2-F-phenyl 2-((cyclopropyl)$_2NCH_2$)phenyl
258. 2-F-phenyl 2-((cyclobutyl)$NHCH_2$)phenyl
259. 2-F-phenyl 2-((cyclobutyl)$_2NCH_2$)phenyl
260. 2-F-phenyl 2-((cyclopentyl)$NHCH_2$)phenyl
261. 2-F-phenyl 2-((cyclopentyl)$_2NCH_2$)phenyl
262. 2-F-phenyl 2-((cyclohexyl)$NHCH_2$)phenyl
263. 2-F-phenyl 2-((cyclohexyl)$_2NCH_2$)phenyl
264. 2-F-phenyl 1-CH_3-2-imidazolyl
265. 2-F-phenyl 2-CH_3-1-imidazolyl
266. 2-F-phenyl 2-((CH_3)$_2NCH_2$)-1-imidazolyl
267. 2-F-phenyl 2-((CH_3)$NHCH_2$)-1-imidazolyl
268. 2-F-phenyl 2-((CH_3CH_2)$NHCH_2$)-1-imidazolyl
269. 2-F-phenyl 2-((CH_3CH_2)$_2NCH_2$)-1-imidazolyl
270. 2-F-phenyl 2-((CH_3CH_2)N(CH_3)CH_2)-1-imidazolyl
271. 2-F-phenyl 2-(((CH_3)$_2$CH)$NHCH_2$)-1-imidazolyl
272. 2-F-phenyl 2-(((CH_3)$_2$CH)$_2NCH_2$)-1-imidazolyl
273. 2-F-phenyl 2-((cyclopropyl)$NHCH_2$)-1-imidazolyl
274. 2-F-phenyl 2-((cyclopropyl)$_2NCH_2$)-1-imidazolyl
275. 2-F-phenyl 2-((cyclobutyl)$NHCH_2$)-1-imidazolyl
276. 2-F-phenyl 2-((cyclobutyl)$_2NCH_2$)-1-imidazolyl
277. 2-F-phenyl 2-((cyclopentyl)$NHCH_2$)-1-imidazolyl
278. 2-F-phenyl 2-((cyclopentyl)$_2NCH_2$)-1-imidazolyl
279. 2-F-phenyl 2-((cyclohexyl)$NHCH_2$)-1-imidazolyl
280. 2-F-phenyl 2-((cyclohexyl)$_2NCH_2$)-1-imidazolyl
281. 2,6-diF-phenyl 2-(NH_2SO_2)phenyl
282. 2,6-diF-phenyl 2-(CH_3SO_2)phenyl
283. 2,6-diF-phenyl 3-NH_2SO_2-4-pyridyl
284. 2,6-diF-phenyl 3-CH_3SO_2-4-pyridyl
285. 2,6-diF-phenyl 2-(CH_3NH)phenyl

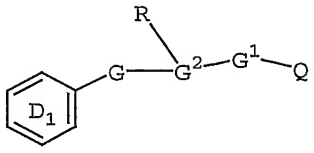
286. 2,6-diF-phenyl 3-((CH3)2NCH2)-4-pyridyl
287. 2,6-diF-phenyl 2-(N-(3-R-HO-pyrrolidinyl)CH2)phenyl
288. 2,6-diF-phenyl 2-(N-(4-HO-piperidinyl)CH2)phenyl
289. 2,6-diF-phenyl 2-((CH3)2NCH2)phenyl
290. 2,6-diF-phenyl 2-((CH3)NHCH2)phenyl
291. 2,6-diF-phenyl 2-((CH3CH2)NHCH2)phenyl
292. 2,6-diF-phenyl 2-((CH3CH2)2NCH2)phenyl
293. 2,6-diF-phenyl 2-((CH3CH2)N(CH3)CH2)phenyl
294. 2,6-diF-phenyl 2-(((CH3)2CH)NHCH2)phenyl
295. 2,6-diF-phenyl 2-(((CH3)2CH)2NCH2)phenyl
296. 2,6-diF-phenyl 2-((cyclopropyl)NHCH2)phenyl
297. 2,6-diF-phenyl 2-((cyclopropyl)2NCH2)phenyl
298. 2,6-diF-phenyl 2-((cyclobutyl)NHCH2)phenyl
299. 2,6-diF-phenyl 2-((cyclobutyl)2NCH2)phenyl
300. 2,6-diF-phenyl 2-((cyclopentyl)NHCH2)phenyl
301. 2,6-diF-phenyl 2-((cyclopentyl)2NCH2)phenyl
302. 2,6-diF-phenyl 2-((cyclohexyl)NHCH2)phenyl
303. 2,6-diF-phenyl 2-((cyclohexyl)2NCH2)phenyl
304. 2,6-diF-phenyl 1-CH3-2-imidazolyl
305. 2,6-diF-phenyl 2-CH3-1-imidazolyl
306. 2,6-diF-phenyl 2-((CH3)2NCH2)-1-imidazolyl
307. 2,6-diF-phenyl 2-((CH3)NHCH2)-1-imidazolyl
308. 2,6-diF-phenyl 2-((CH3CH2)NHCH2)-1-imidazolyl
309. 2,6-diF-phenyl 2-((CH3CH2)2NCH2)-1-imidazolyl
310. 2,6-diF-phenyl 2-((CH3CH2)N(CH3)CH2)-1-imidazolyl
311. 2,6-diF-phenyl 2-(((CH3)2CH)NHCH2)-1-imidazolyl
312. 2,6-diF-phenyl 2-(((CH3)2CH)2NCH2)-1-imidazolyl
313. 2,6-diF-phenyl 2-((cyclopropyl)NHCH2)-1-imidazolyl
314. 2,6-diF-phenyl 2-((cyclopropyl)2NCH2)-1-imidazolyl
315. 2,6-diF-phenyl 2-((cyclobutyl)NHCH2)-1-imidazolyl
316. 2,6-diF-phenyl 2-((cyclobutyl)2NCH2)-1-imidazolyl
317. 2,6-diF-phenyl 2-((cyclopentyl)NHCH2)-1-imidazolyl
318. 2,6-diF-phenyl 2-((cyclopentyl)2NCH2)-1-imidazolyl
319. 2,6-diF-phenyl 2-((cyclohexyl)NHCH2)-1-imidazolyl
320. 2,6-diF-phenyl 2-((cyclohexyl)2NCH2)-1-imidazolyl
321. piperidinyl 2-(NH2SO2)phenyl
322. piperidinyl 2-(CH3SO2)phenyl
323. piperidinyl 3-NH2SO2-4-pyridyl
324. piperidinyl 3-CH3SO2-4-pyridyl
325. piperidinyl 2-(CH3NH)phenyl
326. piperidinyl 3-((CH3)2NCH2)-4-pyridyl
327. piperidinyl 2-(N-(3-R-HO-pyrrolidinyl)CH2)phenyl
328. piperidinyl 2-(N-(4-HO-piperidinyl)CH2)phenyl
329. piperidinyl 2-((CH3)2NCH2)phenyl
330. piperidinyl 2-((CH3)NHCH2)phenyl
331. piperidinyl 2-((CH3CH2)NHCH2)phenyl
332. piperidinyl 2-((CH3CH2)2NCH2)phenyl
333. piperidinyl 2-((CH3CH2)N(CH3)CH2)phenyl
334. piperidinyl 2-(((CH3)2CH)NHCH2)phenyl
335. piperidinyl 2-(((CH3)2CH)2NCH2)phenyl
336. piperidinyl 2-((cyclopropyl)NHCH2)phenyl
337. piperidinyl 2-((cyclopropyl)2NCH2)phenyl
338. piperidinyl 2-((cyclobutyl)NHCH2)phenyl

339. piperidinyl 2-((cyclobutyl)$_2$NCH$_2$)phenyl
340. piperidinyl 2-((cyclopentyl)NHCH$_2$)phenyl
341. piperidinyl 2-((cyclopentyl)$_2$NCH$_2$)phenyl
342. piperidinyl 2-((cyclohexyl)NHCH$_2$)phenyl
343. piperidinyl 2-((cyclohexyl)$_2$NCH$_2$)phenyl
344. piperidinyl 1-CH$_3$-2-imidazolyl
345. piperidinyl 2-CH$_3$-1-imidazolyl
346. piperidinyl 2-((CH$_3$)$_2$NCH$_2$)-1-imidazolyl
347. piperidinyl 2-((CH$_3$)NHCH$_2$)-1-imidazolyl
348. piperidinyl 2-((CH$_3$CH$_2$)NHCH$_2$)-1-imidazolyl
349. piperidinyl 2-((CH$_3$CH$_2$)$_2$NCH$_2$)-1-imidazolyl
350. piperidinyl 2-((CH$_3$CH$_2$)N(CH$_3$)CH$_2$)-1-imidazolyl
351. piperidinyl 2-(((CH$_3$)$_2$CH)NHCH$_2$)-1-imidazolyl
352. piperidinyl 2-(((CH$_3$)$_2$CH)$_2$NCH$_2$)-1-imidazolyl
353. piperidinyl 2-((cyclopropyl)NHCH$_2$)-1-imidazolyl
354. piperidinyl 2-((cyclopropyl)$_2$NCH$_2$)-1-imidazolyl
355. piperidinyl 2-((cyclobutyl)NHCH$_2$)-1-imidazolyl
356. piperidinyl 2-((cyclobutyl)$_2$NCH$_2$)-1-imidazolyl
357. piperidinyl 2-((cyclopentyl)NHCH$_2$)-1-imidazolyl
358. piperidinyl 2-((cyclopentyl)$_2$NCH$_2$)-1-imidazolyl
359. piperidinyl 2-((cyclohexyl)NHCH$_2$)-1-imidazolyl
360. piperidinyl 2-((cyclohexyl)$_2$NCH$_2$)-1-imidazolyl

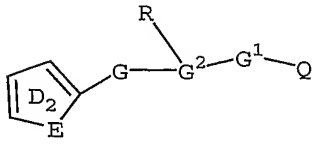
Numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims, the invention may be practiced otherwise that as specifically described herein.

WHAT IS CLAIMED IS:

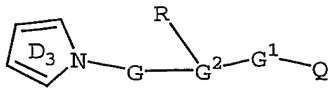
1. A compound of formula Ia, Ib, or Ic:



Ia



Ib



Ic

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

ring D_1 is selected from pyridine, pyrazine, pyridazine, and pyrimidine and is substituted with 1 R^a and 0-1 R^b;

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-3 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

R^a is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$

alkyl)$_2$, C(=NH)NH$_2$, CH$_2$NH$_2$, CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$N(C$_{1-3}$ alkyl)$_2$, CH$_2$CH$_2$NH$_2$, CH$_2$CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$CH$_2$N(C$_{1-3}$ alkyl)$_2$, (CR^{8}R^9)$_t$NR^{7}R^8, (CR^{8}R^9)$_t$C(O)NR^{7}R^8, and OCF$_3$;

R^b is selected from H, C$_{1-4}$ alkyl, F, Cl, Br, I, OH, OCH$_3$, OCH$_2$CH$_3$, OCH(CH$_3$)$_2$, OCH$_2$CH$_2$CH$_3$, CN, C(=NR^8)NR^{7}R^9, NHC(=NR^8)NR^{7}R^9, NR^{8}CH(=NR^7), NH$_2$, NH(C$_{1-3}$ alkyl), N(C$_{1-3}$ alkyl)$_2$, C(=NH)NH$_2$, CH$_2$NH$_2$, CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$N(C$_{1-3}$ alkyl)$_2$, CH$_2$CH$_2$NH$_2$, CH$_2$CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$CH$_2$N(C$_{1-3}$ alkyl)$_2$, (CR^{8}R^9)$_t$NR^{7}R^8, (CR^{8}R^9)$_t$C(O)NR^{7}R^8, and OCF$_3$;

R^c is selected from H, C$_{1-4}$ alkyl, OCH$_3$, OCH$_2$CH$_3$, OCH(CH$_3$)$_2$, OCH$_2$CH$_2$CH$_3$, NH$_2$, NH(C$_{1-3}$ alkyl), N(C$_{1-3}$ alkyl)$_2$, C(=NH)NH$_2$, CH$_2$NH$_2$, CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$N(C$_{1-3}$ alkyl)$_2$, CH$_2$CH$_2$NH$_2$, CH$_2$CH$_2$NH(C$_{1-3}$ alkyl), CH$_2$CH$_2$N(C$_{1-3}$ alkyl)$_2$, (CR^{8}R^9)$_t$NR^{7}R^8, (CR^{8}R^9)$_t$C(O)NR^{7}R^8, and OCF$_3$;

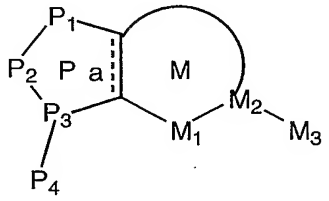
G is absent or is selected from CH$_2$, C(O), O, NR^3, S(O)$_p$, CH$_2$CH$_2$, C(O)CH$_2$, CH$_2$C(O), OCH$_2$, CH$_2$O, NR^{3}CH$_2$, CH$_2$NR^3, S(O)$_p$CH$_2$, CH$_2$S(O)$_p$, CH$_2$CH$_2$CH$_2$, C(O)CH$_2$CH$_2$, CH$_2$C(O)CH$_2$, CH$_2$CH$_2$C(O), OCH$_2$CH$_2$, CH$_2$OCH$_2$, CH$_2$CH$_2$O, NR^{3}CH$_2$CH$_2$, CH$_2$NR^{3}CH$_2$, CH$_2$CH$_2$NR^3, S(O)$_p$CH$_2$CH$_2$, CH$_2$S(O)$_p$CH$_2$, and CH$_2$CH$_2$S(O)$_p$;

G$_1$ is absent or is selected from (CR^{3}R^{3a})$_{1-5}$, (CR^{3}R^{3a})$_{0-2}$CR^3=CR^3(CR^{3}R^{3a})$_{0-2}$, (CR^{3}R^{3a})$_{0-2}$C≡C(CR^{3}R^{3a})$_{0-2}$, (CR^{3}R^{3a})$_u$C(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$C(O)O(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$OC(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$O(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$C(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$OC(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(O)O(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}C(S)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)$_2$(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)NR^3(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$NR^{3}S(O)$_2$(CR^{3}R^{3a})$_w$, (CR^{3}R^{3a})$_u$S(O)$_2$NR^3(CR^{3}R^{3a})$_w$, and (CR^{3}R^{3a})$_u$NR^{3}S(O)$_2$NR^3(CR^{3}R^{3a})$_w$,

wherein u + w total 0, 1, 2, 3, or 4, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

G^2 is phenyl, naphthyl, or a 5-10 membered heteroaryl consisting of carbon atoms and from 1-3 heteroatoms selected from N, O, and S;

Q is a group of formula II:



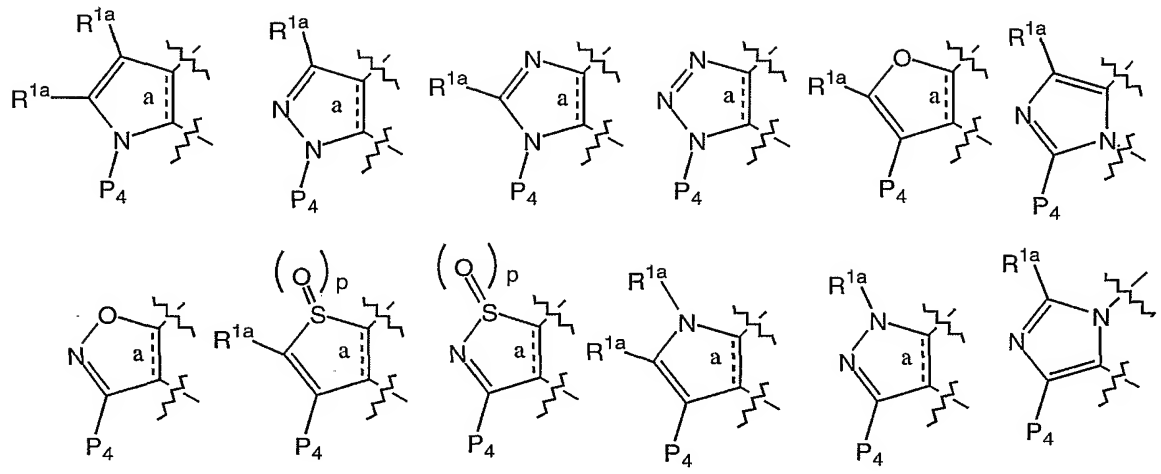
II

one of P_4 and M_3 is -Z-A-B and the other is attached to G_1;

ring M, including M_1 and M_2, is a 6 or 7 membered carbocycle or 6 or 7 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, $S(O)_p$, N, and NZ^2;

ring M is substituted with 0-2 R^{1a} and 0-2 carbonyl groups, and, comprises: 0-2 additional double bonds;

ring P, including P_1, P_2, P_3, and P_4 is selected from group:



"a" is absent or is a bond

provided that when Q is a dihydroimidazolo[4,5-c]-pyridin-4-one then:

(i) G_1 is present and is other than alkylene;

(ii) Z is present and is other than alkylene;

(iii) Ring D_1-G is present, D_1-G is other than benzyloxy;

(iv) Ring D_3 is present; or

(v) Ring D_2 is present and is other than 5-methyl-1,2,4-oxadiazole or 5-oxo-1,2,4-oxadiazole;

Z is selected from a bond, $-(CR^2R^{2a})_{1-4}-$, $(CR^2R^{2a})_qO(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qOC(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)O(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3C(O)NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qS(O)_2(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qSO_2NR^3(CR^2R^{2a})_{q^1}$, $(CR^2R^{2a})_qNR^3SO_2(CR^2R^{2a})_{q^1}$, and $(CR^2R^{2a})_qNR^3SO_2NR^3(CR^2R^{2a})_{q^1}$, wherein $q + q^1$ total 0, 1, or 2, provided that Z does

not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

Z^2 is selected from H, C_{1-4} alkyl, phenyl, benzyl, $C(O)R^3$, and $S(O)_pR^{3c}$;

R^{1a} is selected from H, $-(CH_2)_r-R^{1b}$, $-CH=CH-R^{1b}$, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $NH(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, $S(O)_p(CH_2)_rR^{1d}$, $O(CH_2)_rR^{1d}$, $NR^3(CH_2)_rR^{1d}$, $OC(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)O(CH_2)_rR^{1d}$, and $NR^3C(O)(CH_2)_rR^{1d}$, provided that R^{1a} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

alternatively, when two R^{1a}'s are attached to adjacent atoms, together with the atoms to which they are attached they form a 5-7 membered ring consisting of: carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and $S(O)_p$, this ring being substituted with 0-2 R^{4b} and comprising: 0-3 double bonds;

R^{1b} is selected from H, C_{1-3} alkyl, F, Cl, Br, I, -CN, -CHO, $(CF_2)_rCF_3$, $(CH_2)_rOR^2$, NR^2R^{2a}, $C(O)R^{2c}$, $OC(O)R^2$, $(CF_2)_rCO_2R^{2a}$, $S(O)_pR^{2b}$, $NR^2(CH_2)_rOR^2$, $C(=NR^{2c})NR^2R^{2a}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NHR^{2b}$, $NR^2C(O)_2R^{2a}$, $OC(O)NR^{2a}R^{2b}$, $C(O)NR^2R^{2a}$, $C(O)NR^2(CH_2)_rOR^2$, $SO_2NR^2R^{2a}$, $NR^2SO_2R^{2b}$, C_{3-6} carbocycle substituted with 0-2 R^{4a}, and 5-10 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1b} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

R^{1c} is selected from H, $CH(CH_2OR^2)_2$, $C(O)R^{2c}$, $C(O)NR^2R^{2a}$, $S(O)R^{2b}$, $S(O)_2R^{2b}$, and $SO_2NR^2R^{2a}$;

R^{1d} is selected from C_{3-13} carbocycle substituted with 0-2 R^{4a}, and 5-13 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1d} forms other than an N-N, N-S, or N-O bond;

R^2, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2a}, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, phenethyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2b}, at each occurrence, is selected from CF_3, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2c}, at each occurrence, is selected from CF_3, OH, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue

substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and comprising carbon atoms and from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3a}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3b}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3c}, at each occurrence, is selected from C_{1-4} alkyl, and phenyl;

R^{3d}, at each occurrence, is selected from H, C_{1-4} alkyl, C_{1-4} alkyl-phenyl, and $C(=O)R^{3c}$;

A is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^4, and 5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

X is selected from $-(CR^2R^{2a})_{1-4}-$, $-CR^2(CR^2R^{2b})(CH_2)_t-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-CR^2(OR^2)-$, $-CR^2(SR^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-SCR^2R^{2a}-$, $-S(O)CR^2R^{2a}-$, $-S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S-$, $-CR^2R^{2a}S(O)-$, $-CR^2R^{2a}S(O)_2-$, $-S(O)_2NR^2-$, $-NR^2S(O)_2-$, $-NR^2S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S(O)_2NR^2-$, $-NR^2S(O)_2NR^2-$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)O-$, $-OC(O)NR^2-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^{4a}, and

5-12 membered heterocyclic system comprising carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rN(\rightarrow O)R^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $(CH_2)_rNR^2C(O)R^{2b}$, $(CH_2)_rC(O)NR^2R^{2a}$, $(CH_2)_rNR^2C(O)NR^2R^{2a}$, $(CH_2)_rC(=NR^2)NR^2R^{2a}$, $(CH_2)_rC(=NS(O)_2R^5)NR^2R^{2a}$, $(CH_2)_rNHC(=NR^2)NR^2R^{2a}$, $(CH_2)_rC(O)NHC(=NR^2)NR^2R^{2a}$, $(CH_2)_rSO_2NR^2R^{2a}$, $(CH_2)_rNR^2SO_2NR^2R^{2a}$, $(CH_2)_rNR^2SO_2-C_{1-4}$ alkyl, $(CH_2)_rNR^2SO_2R^5$, $(CH_2)_r-NR^2SO_2R^{5a}$, $(CH_2)_rS(O)_pR^5$, $(CH_2)_r-S(O)_pR^{5a}$, $(CF_2)_rCF_3$, $(CH_2)_r-CF_3$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-NR^{4e}R^{4f}$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-OR^{4e}$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-SR^{4e}$, $(CR^{4c}R^{4d})(CR^{3e}R^{3e})_r-N(\rightarrow O)R^{4e}R^{4f}$, $(CH_2)_rNCH_2R^{1c}$,

$(CH_2)_rOCH_2R^{1c}$, $(CH_2)_rSCH_2R^{1c}$, $(CH_2)_rN(CH_2)_2(CH_2)_tR^{1b}$, $(CH_2)_rO(CH_2)_2(CH_2)_tR^{1b}$, $(CH_2)_rS(CH_2)_2(CH_2)_tR^{1b}$, $(CH_2)_r$5-6 membered carbocycle substituted with 0-1 R^5, and $(CH_2)_r$5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $C(=NS(O)_2R^5)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $C(O)NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, $(CF_2)_rCF_3$, $(CH_2)_r$-CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CF_2)_rCF_3$, $(CH_2)_r$-CF_3, $(CH_2)_r$-F, $(CH_2)_r$-Br, $(CH_2)_r$-Cl, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $(CH_2)_rN=CHOR^3$, $C(O)NH(CH_2)_2NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4b}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^3$, $(CH_2)_r$-F, $(CH_2)_r$-Cl, $(CH_2)_r$-Br, $(CH_2)_r$-I, C_{1-4} alkyl, $(CH_2)_r$-CN, $(CH_2)_r$-NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CH_2)_rCF_3$, and $(CF_2)_rCF_3$;

R^5, at each occurrence, is selected from H, C_{1-6} alkyl, =O, $(CH_2)_rOR^3$, F, Cl, Br, I, -CN, NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $CH(=NOR^{3d})$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CF_2)_rCF_3$, phenyl substituted with 0-2 R^6, naphthyl substituted with 0-2 R^6, and benzyl substituted with 0-2 R^6;

R^6, at each occurrence, is selected from H, OH, $(CH_2)_rOR^2$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2b}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $C(=NH)NH_2$, $NHC(=NH)NH_2$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, and $NR^2SO_2C_{1-4}$ alkyl;

R^7, at each occurrence, is selected from H, OH, C_{1-4} alkoxycarbonyl, C_{6-10} aryloxy, C_{6-10} aryloxycarbonyl, C_{6-10} arylmethylcarbonyl, C_{1-4} alkylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{6-10} arylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, phenylaminocarbonyl, and phenyl C_{1-4} alkoxycarbonyl;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

alternatively, R^7 and R^8, when attached to the same nitrogen, combine to form a 5-6 membered heterocyclic ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

R^9, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

n, at each occurrence, is selected from 0, 1, 2, and 3;

m, at each occurrence, is selected from 0, 1, and 2;

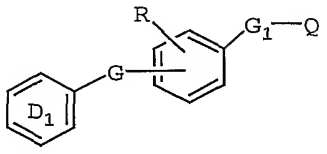
p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3;

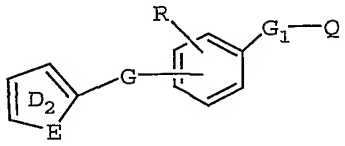
s, at each occurrence, is selected from 0, 1, and 2; and,

t, at each occurrence, is selected from 0, 1, 2, and 3.

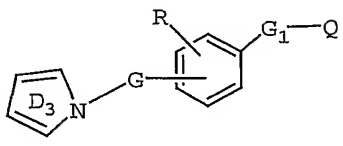
2. A compound according to Claim 1, wherein the compound is of formula Ia_1-Ic_1, wherein:



Ia_1



Ib_1



Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E

is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 R^a and 0-1 R^b;

R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

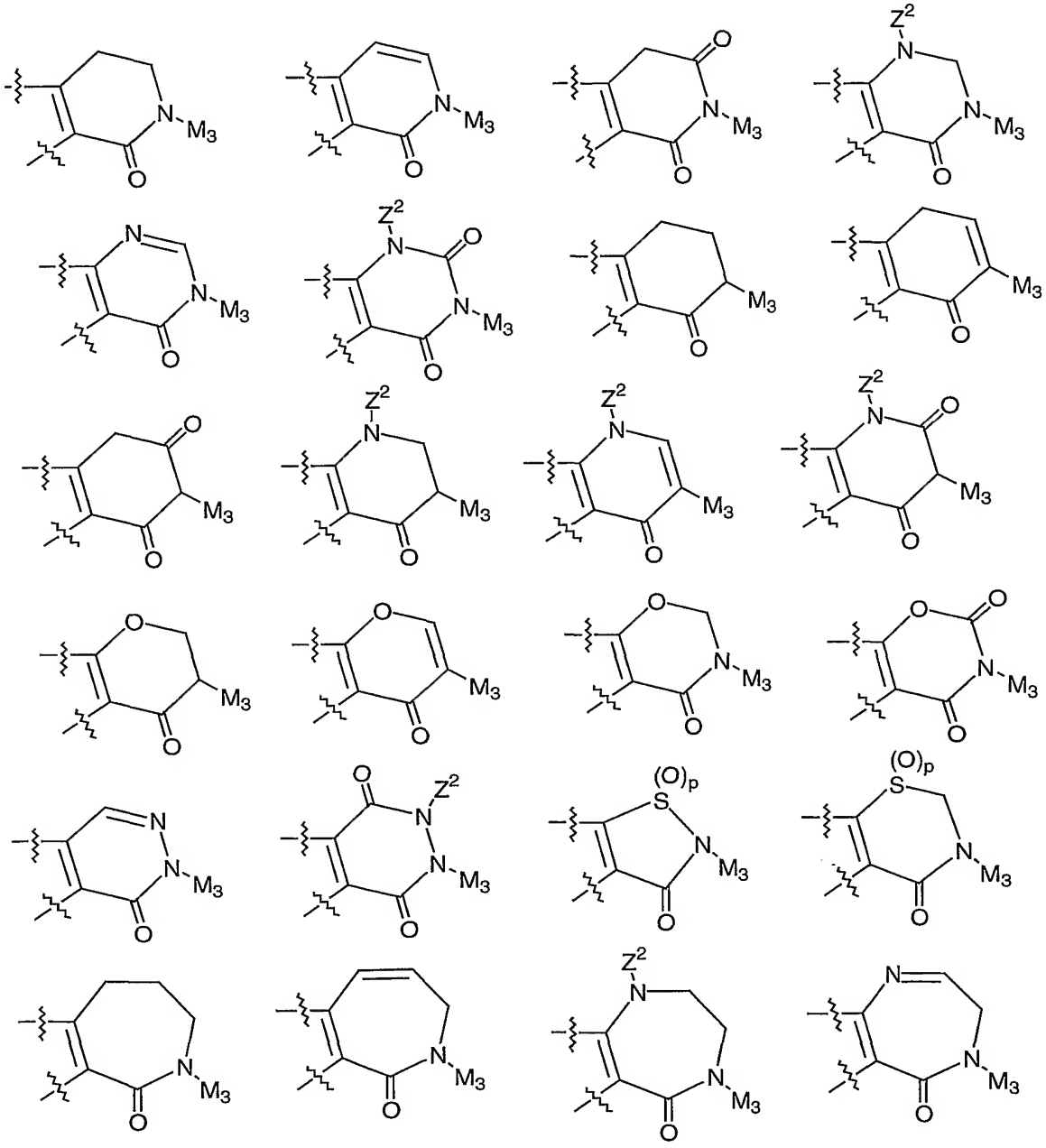
R^a is selected from H, OH, SH, C_{1-3} alkoxy, C_{1-3} thioalkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

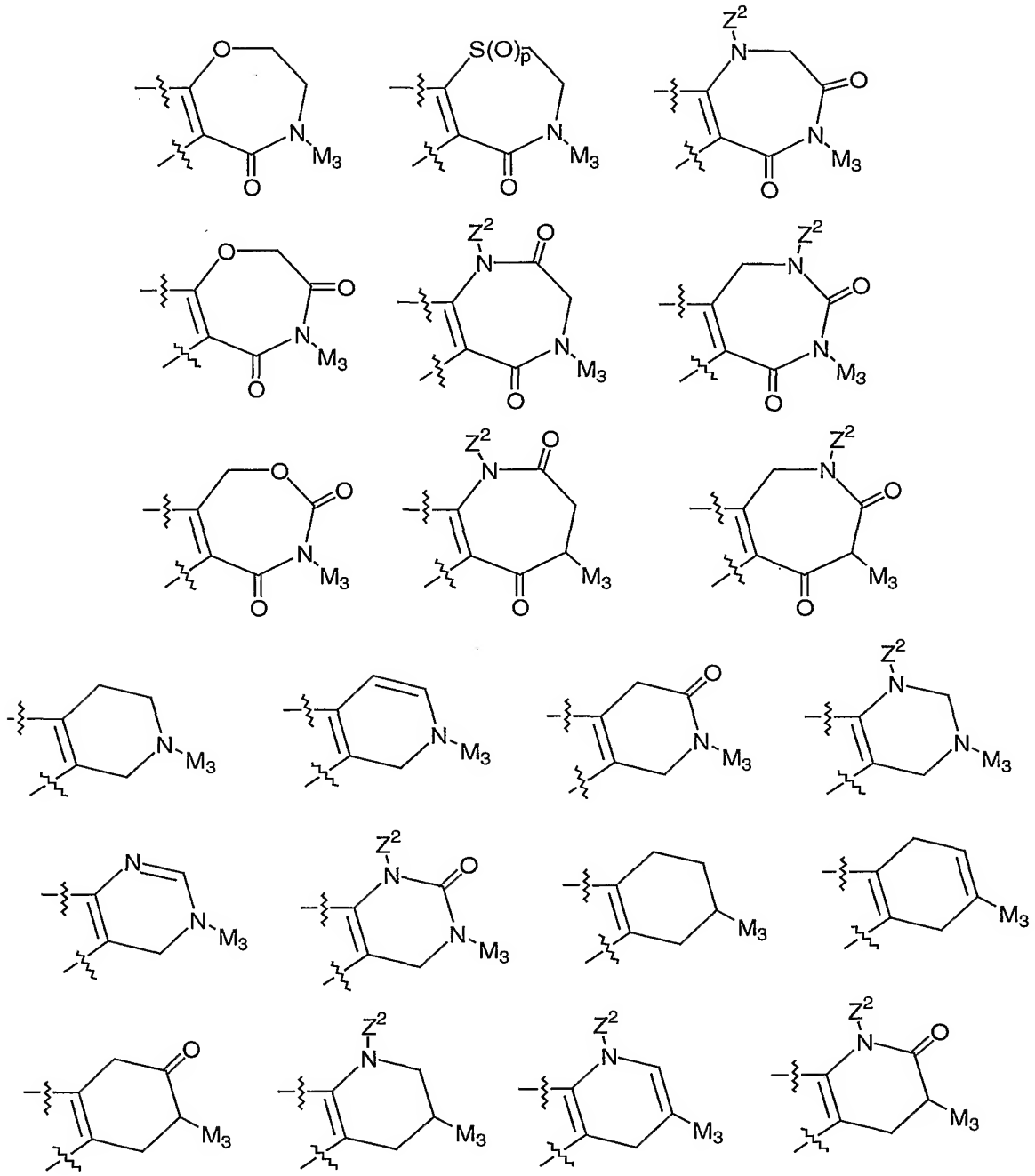
R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

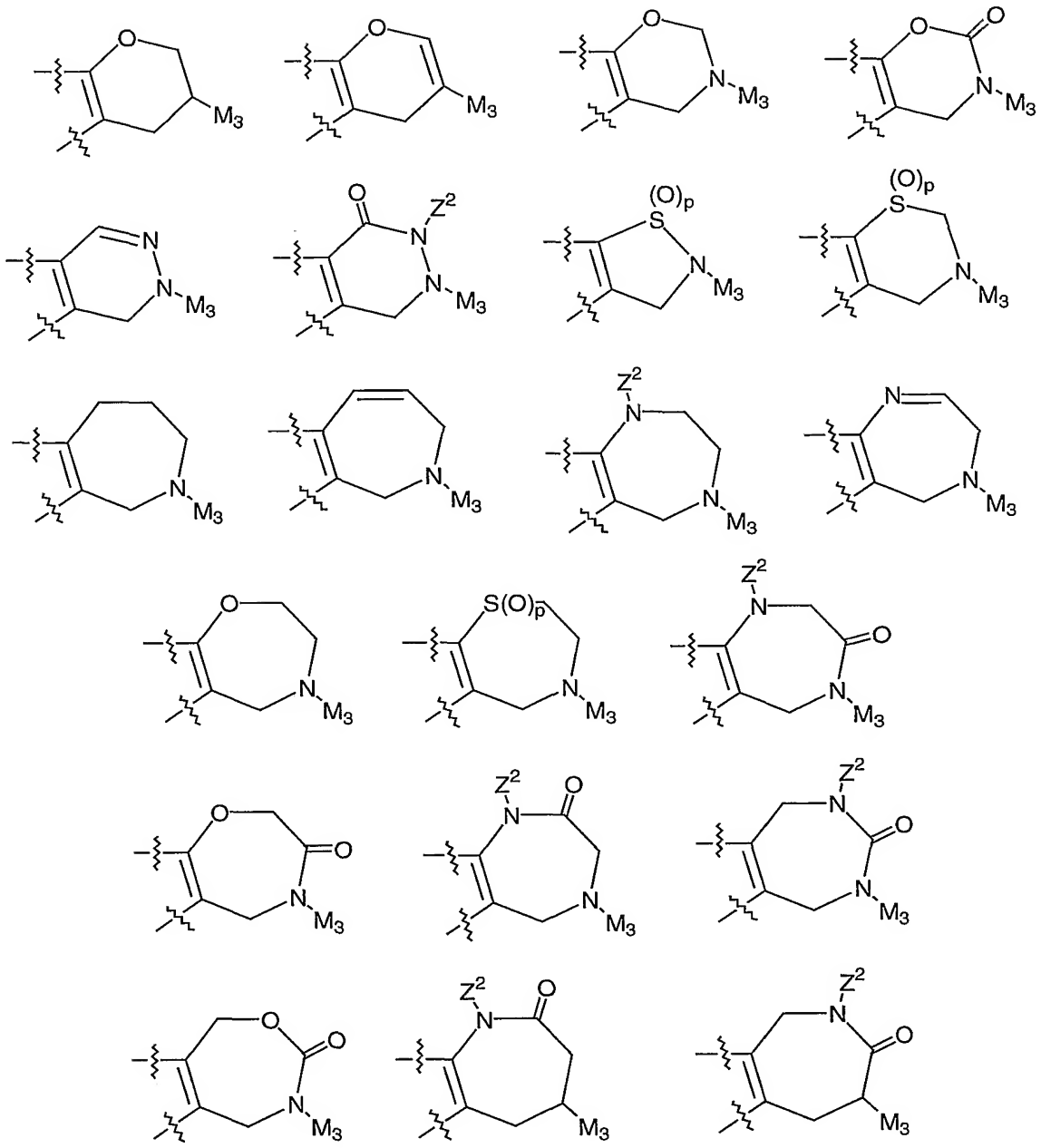
R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

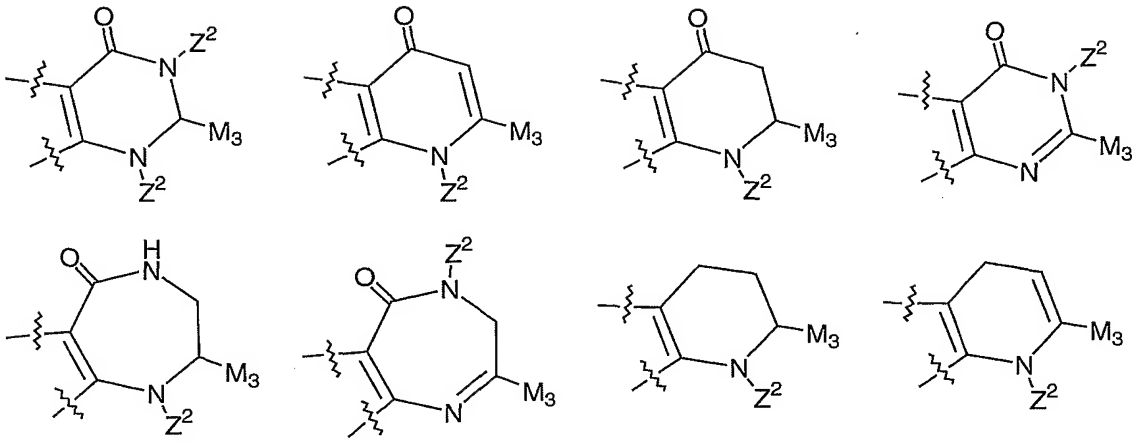
G_1 is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$, and provided that G_1-Q form other than a N-N, O-N, or S-N bond;

ring M is substituted with 0-2 R^{1a} and is selected from the group:



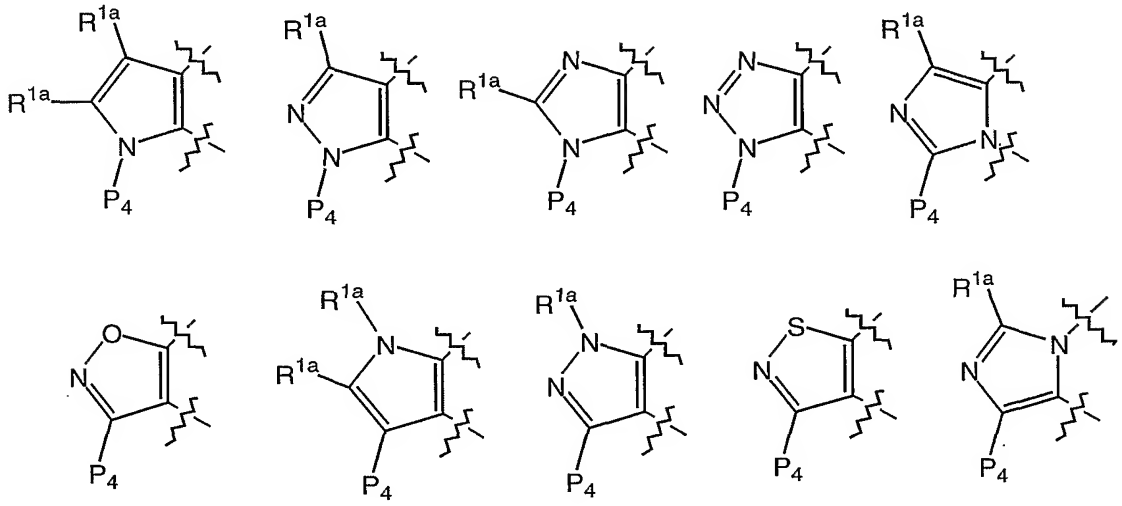






Z^2 is selected from H, C_{1-4} alkyl, phenyl, benzyl, $C(O)R^3$, and $S(O)_pR^{3c}$;

ring P, including P_1, P_2, P_3, and P_4 is selected from group:



G_1 is absent or is selected from $(CR^3R^{3a})_{1-3}$, $(CR^3R^{3a})_uC(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uO(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uC(O)NR^3(CR^3R^{3a})_w$, $(CR^3R^{3a})_uNR^3C(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)_2(CR^3R^{3a})_w$, $(CR^3R^{3a})_uS(O)NR^3(CR^3R^{3a})_w$, and $(CR^3R^{3a})_uS(O)_2NR^3(CR^3R^{3a})_w$, wherein u + w total 0, 1, or 2, provided that G_1 does

not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

A is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^4;

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

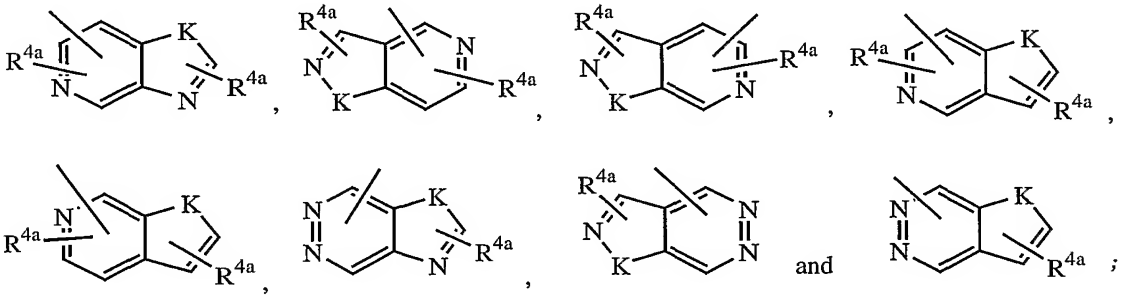
X is selected from $-(CR^2R^{2a})_{1-4}-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from one of the following carbocyclic and heterocyclic systems that are substituted with 0-2 R^{4a};

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl,

1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic heteroaryl ring systems:



K is selected from O, S, NH, and N;

Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, $C(O)NH$, $NHC(O)$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

3. A compound according to Claim 2, wherein the compound is of formula Ib_1 or Ic_1, wherein:

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

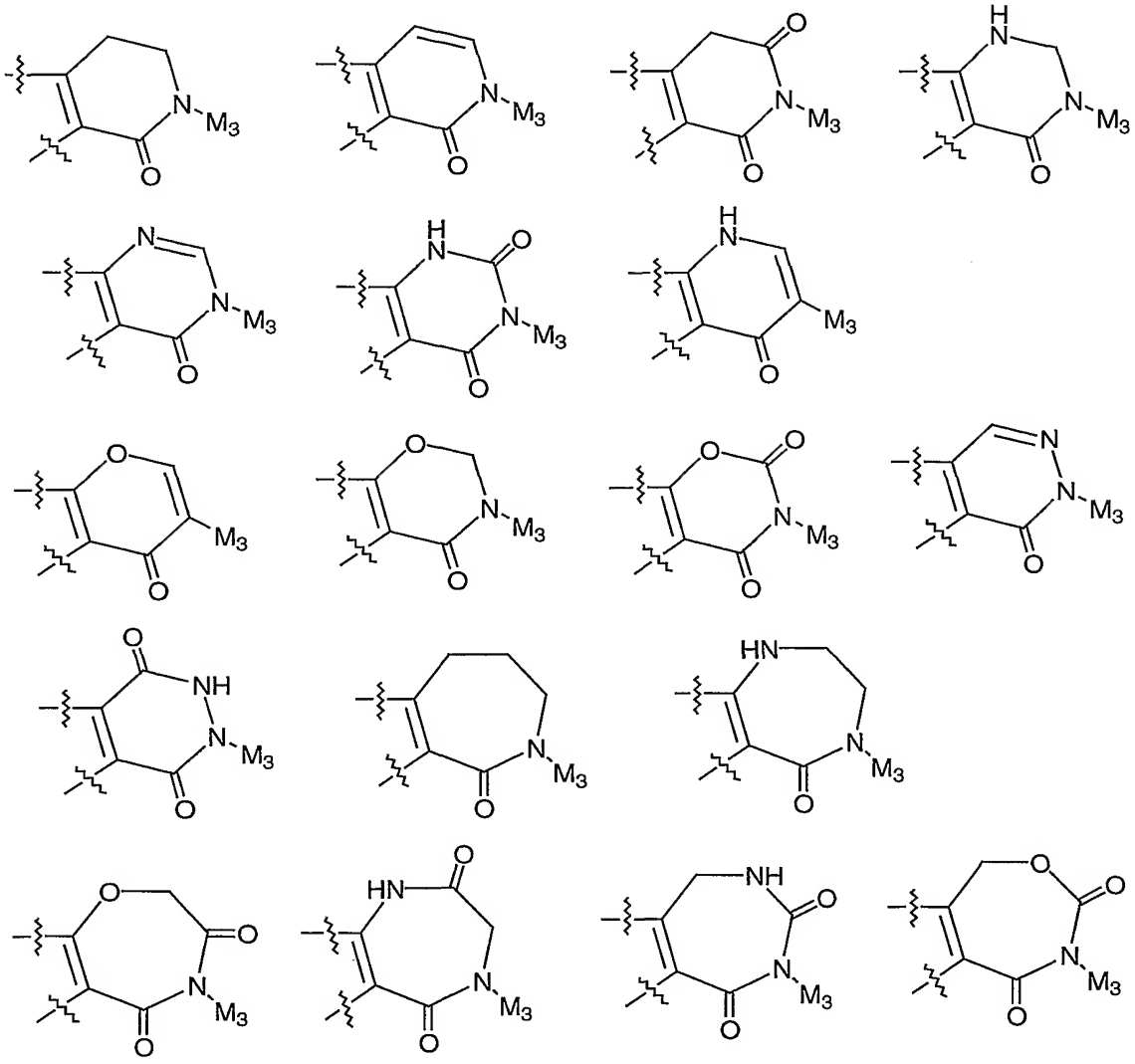
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

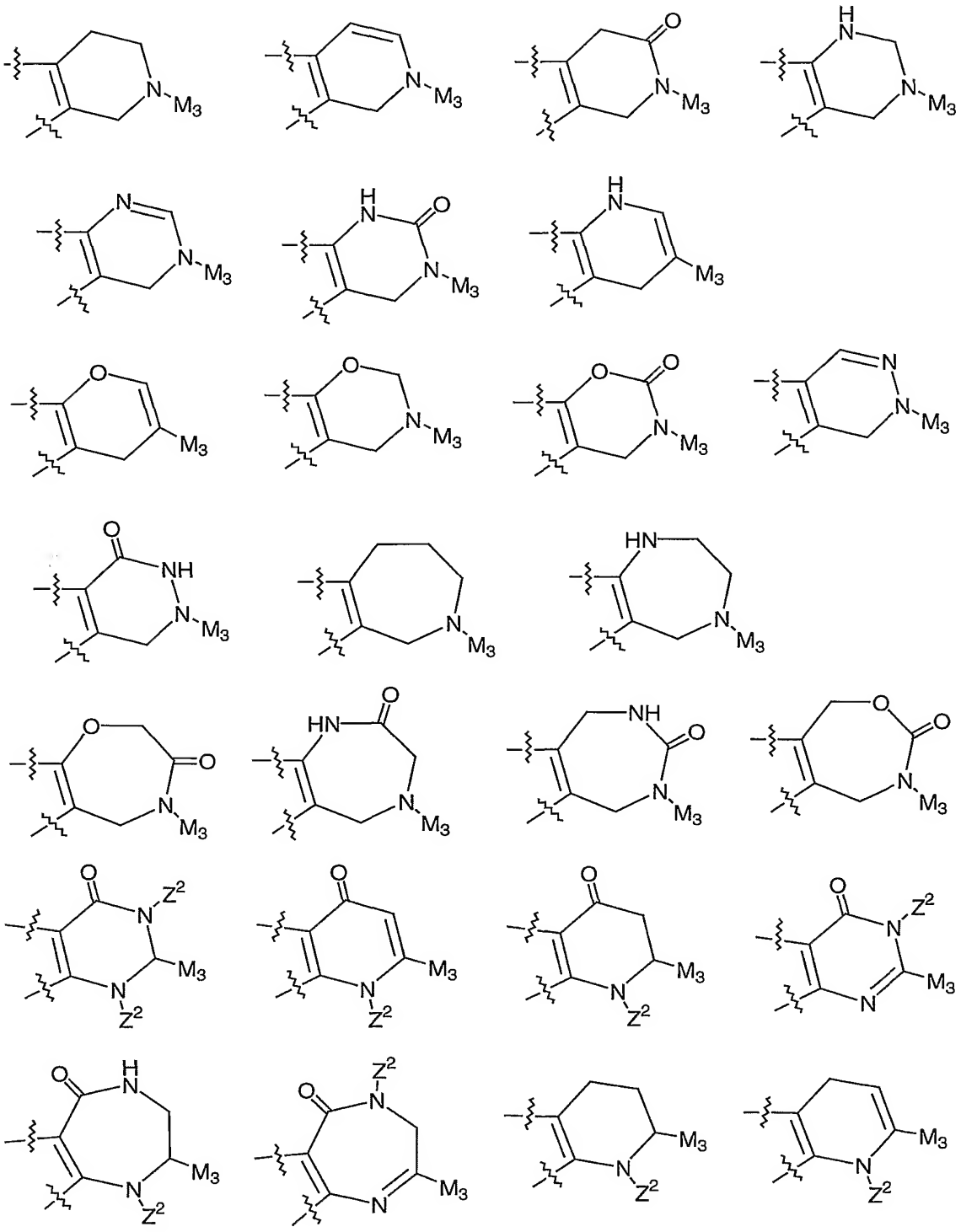
R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

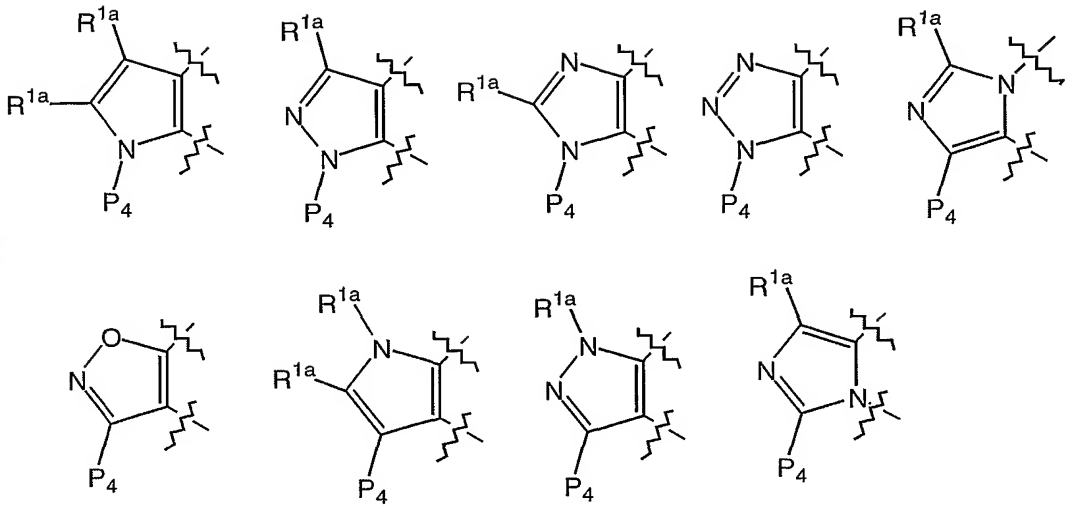
R^c is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

ring M is substituted with 0-2 R^{1a} and is selected from the group:





ring P, including P_1, P_2, P_3, and P_4 is selected from group:



Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran, benzothiofuran, indole, benzimidazole, benzimidazolone, benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole;

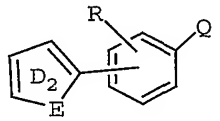
Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, $C(O)NH$, $NHC(O)$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$,

$NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

4. A compound according to Claim 3, wherein the compound is of wherein the compound is of formula Ib_2:



Ib_2

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

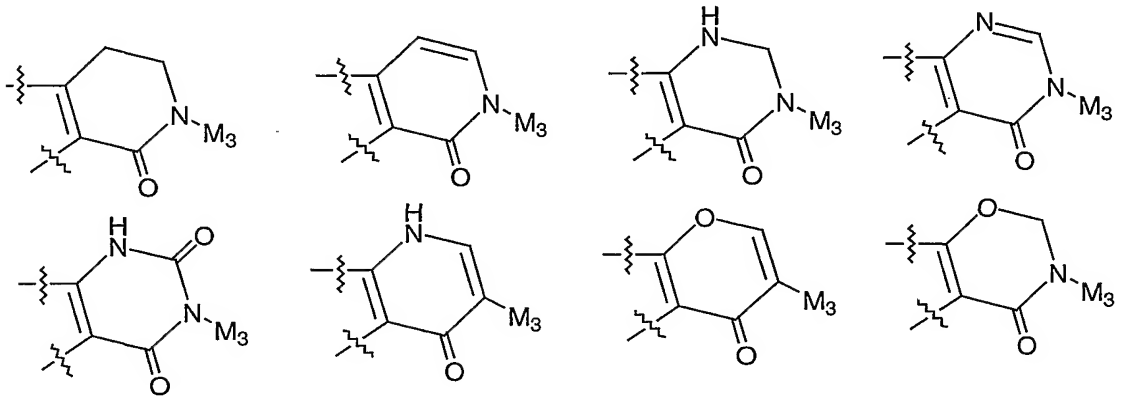
ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N- R^c and ring D_2 is substituted with 1 R^a and 0-1 R^b;

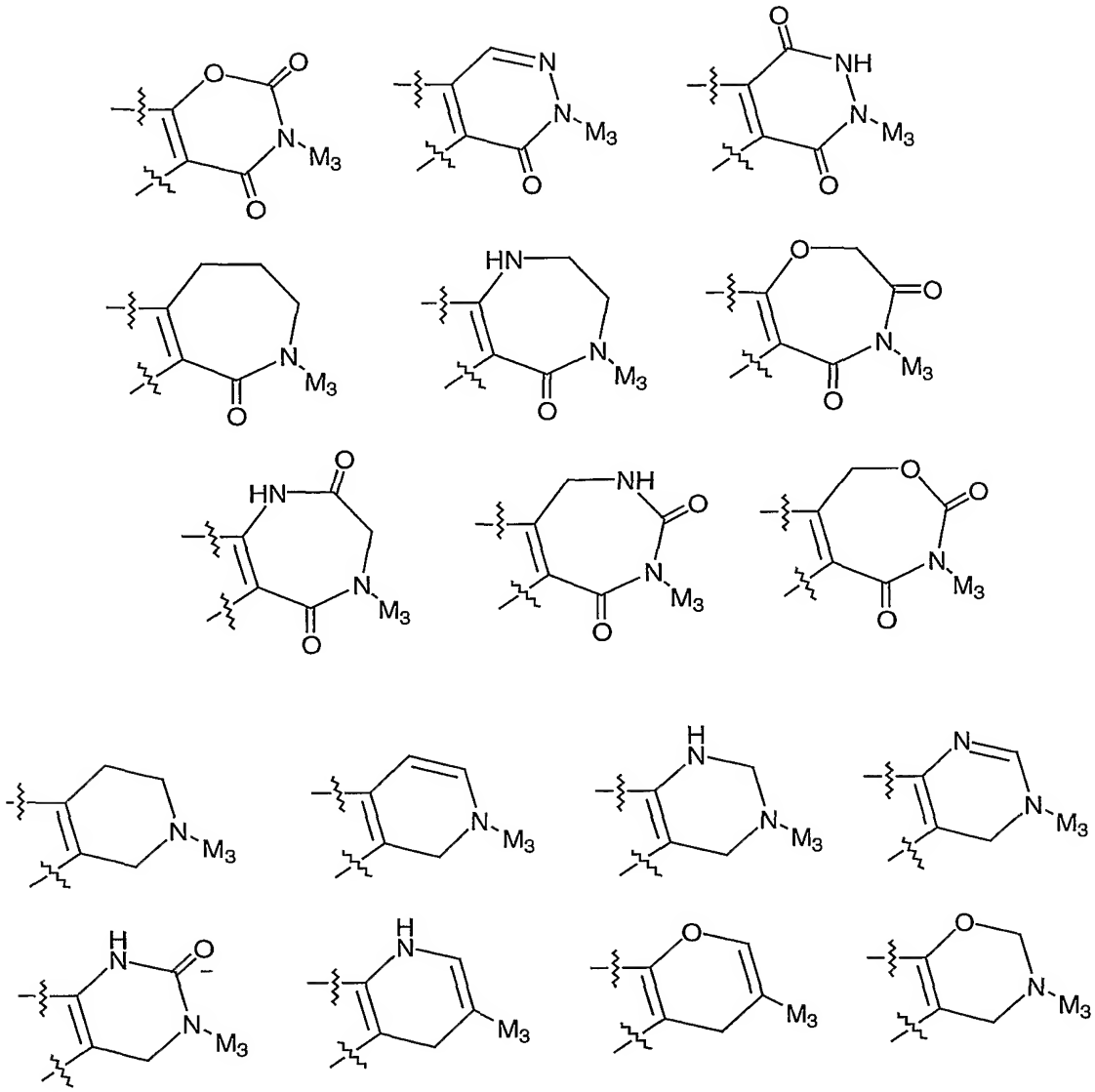
R is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

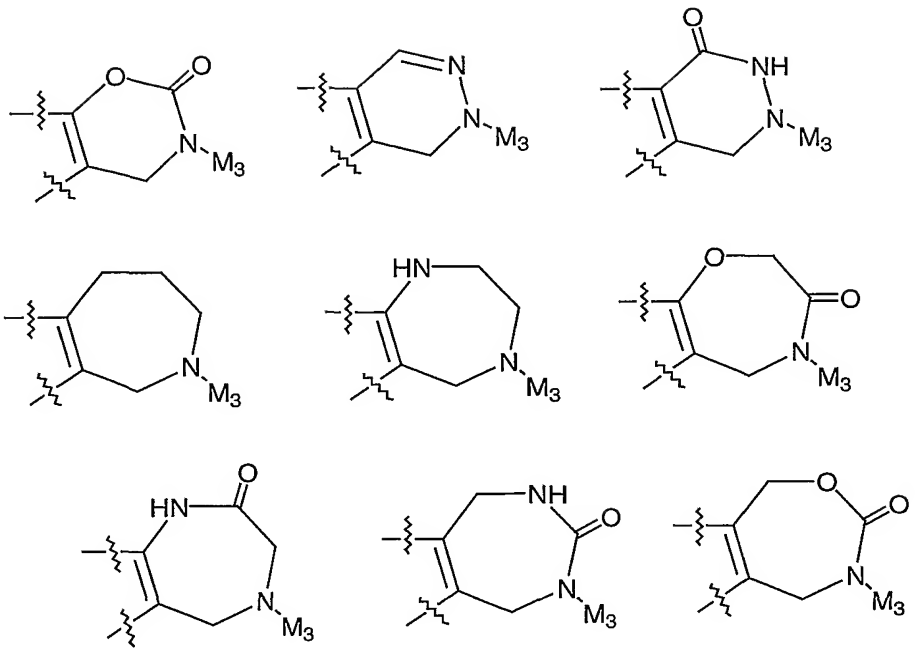
R^a is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), and $N(C_{1-3}$ alkyl)$_2$;

R^b is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

ring M is substituted with 0-1 R^{1a} and is selected from the group:

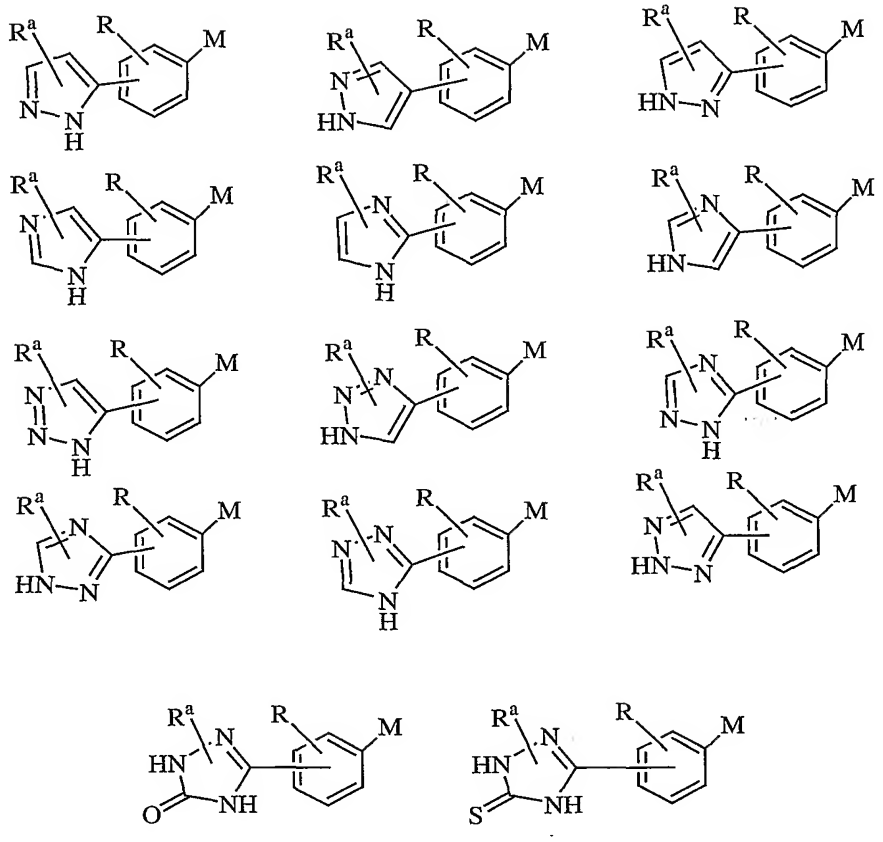






G_1 is absent or is selected from CH_2, CH_2CH_2, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, $C(O)NH$, $NHC(O)$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that G_1 does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached.

5. A compound according to Claim 4, wherein the compound is selected from one of the formulas:



or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

G_1 is absent;

A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R^4; and,

B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R^{4a};

R^2, at each occurrence, is selected from H, CH_3, CH_2CH_3, cyclopropylmethyl, cyclobutyl, and cyclopentyl;

R^{2a}, at each occurrence, is selected from H, CH_3, and CH_2CH_3;

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form pyrrolidine substituted with 0-2 R^{4b} or piperidine substituted with 0-2 R^{4b};

R^4, at each occurrence, is selected from OH, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, F, Br, Cl, I, C_{1-4} alkyl, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, CF_3, and $(CF_2)CF_3$;

R^{4a} is selected from C_{1-4} alkyl, CF_3, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, SR^5, $S(O)R^5$, $S(O)_2R^5$, $SO_2NR^2R^{2a}$, and 1-CF_3-tetrazol-2-yl;

R^{4b}, at each occurrence, is selected from H, CH_3, and OH;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl; and,

r, at each occurrence, is selected from 0, 1, and 2.

6. A compound according to Claim 5, wherein:

A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl; and,

B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-

methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

7. A compound according to Claim 1, wherein the compound is selected from the group:

1-[3-(2'-Amino-3',4'-thiadiazol-5'-yl)phenyl]-3-methyl-6-[2'-aminosulfonyl-[1,1']-biphen-4-yl]-1,4,5,6-tetrahydropyrazolo-[3,4-*c*]-pyridin-7-one trifluoroacetic acid salt;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-

pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-

fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4-dihydropyrazolo-[4,3-d]-pyrimidine-5,7-dione;

or a pharmaceutically acceptable salt thereof.

8. A compound according to Claim 1, wherein the compound is selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-

biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-

biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyrimidin-7-one;

or a pharmaceutically acceptable salt thereof.

9. A compound according to Claim 1, wherein the compound is selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-

biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,6-dihydropyrazolo-[4,3-d]-pyridazin-7-one;

or a pharmaceutically acceptable salt thereof.

10. A compound according to Claim 1, wherein the compound is selected from the group:

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N,N-dimethylaminomethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-N-pyrrolidinylmethyl-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[(2'-(3"-hydroxy-N-pyrrolidinylmethyl)-[1,1']-biphen-4-yl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-

fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-

fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-(N,N-dimethylamino)methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(1',3',4'-Triazol-2'-on-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-3',4'-oxadiazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(2'-Amino-1',3',4'-triazol-5'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-3'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-cyano-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-trifluoromethyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

1-[3-(Pyrid-4'-yl)phenyl]-3-(ethoxycarbonyl)-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one; and,

1-[3-(Pyrid-4'-yl)phenyl]-3-methyl-6-[4-(2'-methylimidazol-1'-yl)-2-fluorophenyl)aminocarbonyl]-1,4,5,6-tetrahydropyrazolo-[3,4-c]-pyridin-7-one;

or a pharmaceutically acceptable salt thereof.

11. A compound according to Claim 1, wherein the compound is selected from the group:

1-[3-(5-oxo-4,5-Dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-(2'-{[(3*S*)-3-Hydroxy-1-pyrrolidinyl]methyl}-1,1'-biphenyl-4-yl)-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-{2'-[(Dimethylamino)methyl]-1,1'-biphenyl-4-yl}-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-[2'-(Methylsulfonyl)-1,1'-biphenyl-4-yl]-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-oxadiazol-2-yl)phenyl]-6-{2'-[(dimethylamino)methyl]-1,1'-biphenyl-4-yl}-3-

(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-{2'-[(dimethylamino)methyl]-1,1'-biphenyl-4-yl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-(4-{2-[(dimethylamino)methyl]-1*H*-imidazol-1-yl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

1-[3-(5-Amino-1,3,4-thiadiazol-2-yl)phenyl]-6-{4-[2-(1-pyrrolidinylmethyl)-1*H*-imidazol-1-yl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

6-(4-{2-[(Dimethylamino)methyl]-1*H*-imidazol-1-yl}phenyl)-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

3-Methyl-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-{4-[2-(1-pyrrolidinylmethyl)-1*H*-imidazol-1-yl]phenyl}-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

7-Oxo-1-[3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-

4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-[3-(5-Oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-7-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-4,5,6,7-tetrahydropyrazolo[3,4-*c*]azepin-8(1*H*)-one; and,

1-[2-(5-Oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)phenyl]-6-[2'-(1-pyrrolidinylmethyl)-1,1'-biphenyl-4-yl]-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 or a pharmaceutically acceptable salt form thereof.

13. A method for treating or preventing a thromboembolic disorder, comprising: administering, to a patient in need thereof, a therapeutically effective amount of a compound of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 or a pharmaceutically acceptable salt form thereof.

14. A compound of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 for use in therapy.

15. Use of a compound of Claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 for the manufacture of a medicament for the treatment of a thromboembolic disorder.

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 01/20113

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D471/04 C07D487/04 A61K31/415 //(C07D471/04,231:00, 221:00),(C07D487/04,239:00,231:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 57937 A (DU PONT MERCK PHARMA) 23 December 1998 (1998-12-23) cited in the application page 191; claims	7-15
Y	WO 00 20416 A (BERNOTAT DANIELOWSKI SABINE ;MERCK PATENT GMBH (DE); DORSCH DIETER) 13 April 2000 (2000-04-13) cited in the application abstract; claims	7-15
Y	WO 97 23212 A (DU PONT MERCK PHARMA) 3 July 1997 (1997-07-03) cited in the application compounds IIIa, claim 1	7-15

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 October 2001	11/10/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Frelon, D

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INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 01/20113

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 50255 A (DU PONT PHARM CO) 7 October 1999 (1999-10-07) compounds (I), claim 1	7-15
A,P	WO 00 40583 A (BERNOTAT DANIELOWSKI SABINE ;MERCK PATENT GMBH (DE); DORSCH DIETER) 13 July 2000 (2000-07-13) cited in the application abstract; claims	7-15
A,P	WO 00 39131 A (DU PONT PHARM CO) 6 July 2000 (2000-07-06) abstract; claims	7-15
T	FEVIG J M ET AL: "Synthesis and SAR of benzamidine factor Xa inhibitors containing a vicinally-substituted heterocyclic core" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 11, no. 5, 12 March 2001 (2001-03-12), pages 641-645, XP004230080 ISSN: 0960-894X the whole document	7-15

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-6,12-15(part)

Present claims 1-6,12-15 relate to an extremely large number of possible compounds. In fact, so many options, variables, possible permutations and combinations result in a claimed subject-matter that is so broad in scope that it is rendered virtually incomprehensible and therefore very difficult, if not impossible, to determine the matter for which a protection might legitimately be sought (Art. 6 PCT).
Note also that the claimed subject-matter lacks a significant structural element qualifying as the special technical feature that clearly defines a contribution over the art.

Support within the meaning of Art. 6 PCT and disclosure within the meaning of Art. 5 PCT is to be found, however, for only a selection of the compounds. The present application fails to comply with the clarity, conciseness, support and disclosure requirements of the PCT to such an extent that a meaningful search of the claims is impossible.
Consequently, the search has been carried out for those parts of the application which do appear to be clear, concise and supported by the description, namely those parts relating to the compounds specified in the examples and the compounds claimed in claims 7 to 11, i.e., 1-(heteroaryl-3-phenyl)-pyrazolo(pyridin- or pyrimidin- or pyridazin)-7-one and/or 1-(heteroaryl-3-phenyl)-pyrazoloazepin-8-one derivatives.

Note that certain claimed condensations between rings P and M are not possible.
The reasons of some provisos are not clear.
Note additionally that claim 2 is not searchable since it claims two different definitions for the same group G1 (page 205 and 209).
In claim 4, according to the given formula Ib2, G1 should be absent and therefore cannot be given a definition like on page 219.
Claim 5 (and claim 6 depending thereon) lacks also consistency where the group M is not defined as a substituent whereas the same symbol M is used in preceeding claims for a condensed ring.
Even if M were meant for Q (= (P/M)), claim 5 remains unsearchable by referring implicitely to two different claims: to claim 4 for the definition of M and to claim 3 for P, this is a contravention of Rule 6.4 PCT, 2nd sentence.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In ional Application No
PCT/US 01/20113

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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